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STAPLES

BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 3 1953

TREATMENT OF CANCER OF THE LARYNX BY INTERSTITIAL RADIUM NEEDLES

BY

W. DOUGLAS HARMER, M.C., F.R.C.S.

Consulting Surgeon to the Throat Department, St. Bartholomew's Hospital; Consulting Surgeon to Mount Vernon Hospital and the Radium Institute

The object of this investigation was to ascertain the value of interstitial radium needles in the treatment of cancer of the larynx and to compare it with other methods. This subject has not received as much attention as it deserves. Since 1924 120 patients have had operations with the help and advice of colleagues in the cancer departments of St. Bartholomew's Hospital, Mount Vernon Hospital, and the Radium Institute.

In so limited a space it is not possible to name all the "happy band of brothers," but I am especially indebted to Finzi for suggesting that the method should be tried, to Stanford Cade for his valuable advice and co-operation during at least 20 years, and to a number of distinguished physicists, particularly Gray and Neary, who have planned the method of delivering the best dose to the different parts of the larynx, and lastly to my son, who has helped me in the preparation of this paper.

All these patients have been followed up, with the exception of two who left the country within a few months of their treatment and who have been omitted: in one the growth had already disappeared, so that the outlook was favourable, and the other, with an advanced growth, has been assumed to have died of cancer.

Up-to-date reports of all these are recorded. A few that were lost after five years have been listed to the date of their last record.

Clinical Features

Before describing details of treatments some remarks about these cancers are advisable.

Aetiology.—Cancer of the larynx occurs chiefly in males (only 13% in females). Most of our patients were between the ages of 50 and 65. The oldest was 78; the youngest 20. During 55 years in practice I know of only one earlier case—that of a boy of 9½, seen recently in consultation with Mr. James Crooks, who performed a laryngo-fissure and who has since published this interesting case, which I have not included in my series. Nothing was discovered about causation, but a number of these patients stated that their symptoms started after influenza, and one young woman, who was apparently cured by radium needles for two years, had a rapid recurrence following a pregnancy and died in six months. Normally intrinsic cancer grows slowly, but the rate of growth is quite unpredictable. Thus, a patient from India with hoarseness for about a month had a small localized lesion like a simple wart. As the section showed carcinoma he was treated by laryngo-fissure and the whole of his vocal cord was removed. His wife was assured that the outlook was excellent. In a short time, however, it became obvious that the disease had not been arrested, and he died six months later with large metastases in the cervical lymph nodes. The same may happen with growths elsewhere in the throat. A doctor had a small pedunculated wart the size of a pea on his tongue which looked like a simple papilloma. The biopsy report stated, "No evidence of carcinoma." Bilateral metastases were noted soon afterwards and grew rapidly, and when he died in six months they were as large as hens' eggs. Small pedunculated lesions in the upper air passages may be very malignant and incurable.

Symptoms.—It has long been accepted that the shorter the history of hoarseness the better the outlook, but, strangely enough, this statement is not always reliable. Table I gives the histories in 89 patients. It shows surprisingly little variation in survivals after three months. Although the numbers are small it is still not clear why this should be so. It seems that the outlook depends more on situation, type of lesion, and resistance to cancer. A man with a short history may be more difficult to cure than another who has had trouble for years. Incidentally, people who have lived in the Tropics for many years, who have led a sedentary life, or who have eaten and drunk too much seldom survive for long. On the other hand, another patient with 15 years' hoarseness and a very extensive growth involving the cartilages on both sides was needled and lived free of disease for 10 years. Presumably, a patient's resistance to cancer may be lower at the beginning of the disease than after a number of years. Whatever the explanation, some patients respond surprisingly well and others put up no fight at all.

TABLE I.—*Length of History*

	Months				Years							
	<3	3	6	9	1	2	3	4	5	7	10	15
No. of cases . .	2	19	15	11	11	16	6	4	1	2	1	1
3-year survivals	0	11	6	5	5	7	2	2	0	0	0	1

Situation.—It is not known why cancer in one part of the larynx can be cured so easily whereas with a similar growth in another place a patient rarely survives for long. A good instance is cancer of the epiglottis: on the tip it may be so comparatively innocent that it can safely be treated with transoral diathermy excision, while on the base it is a dangerously malignant cancer which can seldom be cured even by wide laryngectomy. It is therefore enormously important to know how the disease behaves in different situations.

Biopsy.—This should always be made, and be repeated if necessary. The report may be negative. Several of our patients required three or more biopsies. If the disease is clinically malignant it should be treated as such. No patients had sarcoma, and personally I have seen only two cases. Generally speaking, the low-grade cancer has the best prognosis, but in the larynx the situation is more important that the histology. Most of our cases had biopsies. Many years after needling, Dr. Ruth Pearson examined the sections of 48 patients at my request and attempted to foretell the outcome according to Broders's grading. The results are expressed in Table II, which appears to show that, contrary to present-day opinion, grading is of considerable value.

TABLE II

	No. of Cases	Clinical Stage		Outcome	
		Early	Advanced	Lived or Died Free of Cancer	Died of Cancer
Broders's stages 1 and 2	24	6	18	15	9
" " 3 " 4	24	5	19	9	15

Clinical Stages

There are three main stages :

I. Early Intrinsic

(37 patients—31% of total reported.) Here the lesion is strictly confined inside the cavity of the larynx. It is usually a small, slowly growing warty lesion localized to the anterior part of the vocal cord and occasionally spreading to the anterior commissure or to the opposite cord. It involves the mucous membrane only, and can often be stripped off without damaging the muscles of the cord (Fig. 1). In fact, when doing a biopsy it is important not to bite too deeply for fear of making a notch which may damage the voice permanently. In rare cases a growth may be hard and ulcerated, which is a more serious condition. If the lesion extends below the cord it is no longer a stage I type. Early lesions often grow slowly and have long histories of hoarseness. They never invade the cervical lymph nodes. At least 80% are curable.

FIG. 1.—Stage I. Early intrinsic.

II. Advanced Intrinsic

(72 patients—62% of total reported.) When first examined these growths are nearly all very advanced, but without enlarged nodes. Incidentally, it is extremely difficult to decide how localized they are, particularly when the cord is immobile. Usually the whole vocal cord is involved and the lesion sometimes spreads to the anterior commissure, the base of the epiglottis, the arytenoid or subglottic space (Fig. 2). Sixty were unilateral, while twelve of them had bilateral lesions which had spread across the anterior or, rarely, the posterior commissures. Eight of these had no tenderness or external swelling, but, when exposed, the growths had perforated the membranes and invaded or softened the cartilages, usually at the lower border of the thyroid cartilage or through the crico-thyroid membrane. Only one of them was cured for six years. Fig. 3 shows such a case in which a localized lesion which seemed superficial was found at operation to have penetrated the cartilage and so could not be included in stage II.

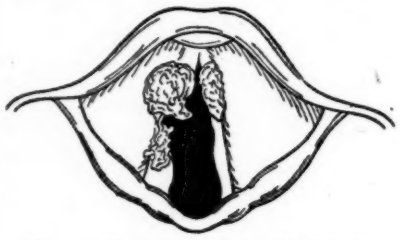
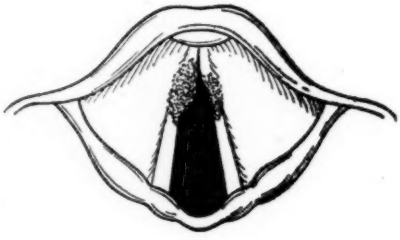


FIG. 2.—Stage II. Advanced intrinsic.

Clinically, there are two groups which help to decide the treatment. (*a*) The large, soft, cauliflower, non-ulcerated type, with a freely movable vocal cord and therefore no deep infiltration. Radium needling should be tried before laryngectomy. Thirty-three patients were treated, many with good results. (*b*) The hard, nodular, ulcerated type with a fixed cord, which signifies deep extension of the disease. Without operation it is impossible to determine how serious this is, but 39 were deliberately treated and some of them were cured. Nearly all these lesions were temporarily improved, and the ulceration usually disappeared.



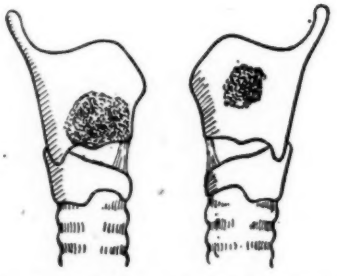


FIG. 3.—Apparently intrinsic (stage II) found at operation to be perforating thyroid cartilage (stage III).

The neck should always be examined to ascertain if there is any external swelling or thickening of the larynx. If on firm pressure the patient complains of tenderness or pain on the affected side, perichondritis should be suspected.

III. Extrinsic

(9 patients—7% of total reported.) Here the lesion is no longer confined inside the larynx. Two different types must be included.

(*a*) The growth which starts in the larynx and then spreads upwards to the base of the epiglottis or tongue or over the lateral fold to involve the pharynx or pyriform fossa, below the vocal cord to the subglottic space or trachea, posteriorly to the arytenoid cartilage or to the post-cricoid region (Fig. 4). All such cancers progress rapidly, and these patients seldom survive for more than a year if untreated.

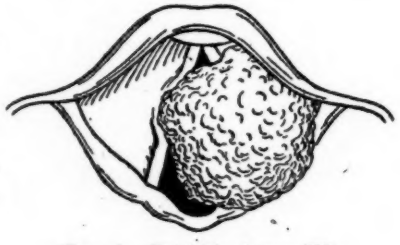


FIG. 4.—Extrinsic (stage III).

(*b*) Here the cancer starts either on the margin of the larynx or on the neighbouring part of the pharynx, spreading later into the larynx.

In the 1945 annual report of the B.E.C.C. dealing with extensive cancer of the larynx, the site of origin was given as follows :

Pyriform fossa	males	137	..	females	12
Post-cricoid space	„	22	..	„	68
Aryepiglottic fold ..	„	42	..	„	4
Vallecula and epiglottis ..	„	61	..	„	4

Such growths are always very malignant and progress rapidly, and the patients rarely live (untreated) for as much as a year. Involvement of the lymphatic nodes is common. The same report described : no nodes, 49 ; enlarged nodes, 81 ; nodes and adjacent tissues involved, 244 ; distant metastases, 9. To emphasize their virulence it was stated that, in spite of treatment, chiefly irradiation, only 15 cases survived for five years. With modern treatments much better results are now obtained.

Choice of Treatment

These can be considered historically. The first attempt to cure cancer was naturally by surgery.

Laryngectomy

In 1863 the first laryngectomy for papillomata was performed by Sands (Canada) ; in 1866 Patrick Watson (Edinburgh) removed a larynx for syphilis ; and in 1873 Czerney and Billroth performed another laryngectomy for cancer. In 1887 the German Crown Prince contracted cancer, and von Bergmann advised this operation. When pressed, this great surgeon said that he had performed it seven times, with an average survival of 19 days. His advice was not accepted. But the prince's illness caused enormous controversy and Queen Victoria sent Morell Mackenzie to advise her son-in-law, greatly to the annoyance of the German surgeons, who walked out. The prince lived for just under a year, long enough to become emperor.

The years 1870 to 1900 can be described as the age of laryngectomy. During this period many larynges were removed, but nearly all the patients died of bronchopneumonia, sepsis, and heart failure. With antibiotics and modern anaesthesia laryngectomy can now be safely performed by surgeons who have sufficient experience of this operation. The mortality should be 2 to 3% provided the general health of the patient is good. It has always been a popular operation for all stages of the disease, and it is still regarded by many surgeons as preferable to other methods, particularly in Europe and America. But it is still a difficult operation for general surgeons, and for the patient is a great handicap. No patient should be told that it is the only safe treatment ; nor can it be pretended that it will make no difference, for it often causes great depression. The patient should realize that only about 15% of them get good voices.

To-day there are simpler treatments which can safely be tried first. Without doubt laryngectomy is quite unnecessary for early lesions ; before long it may even be found that radiotherapy in some form may cure a number of advanced cancers, and it will not be surprising if pre-operative ray treatments make laryngectomy more successful. For extensive cancer it is a very good treatment. Recently there have been improvements in technique and it has been found that the best results can be obtained only by very wide excisions, with removal of enlarged cervical lymph nodes in one block, preferably at the same operation. To be successful the sterno-mastoid muscles are usually removed. The internal jugular vein is tied on the affected side. Some surgeons now tie both veins. Even very extensive disease involving the pharynx, post-cricoid region, and nodes can now be treated successfully by laryngo-oesophago-pharyngectomy.

Laryngo-fissure

In 1900 Butlin and Semon published a paper showing that "thyrotomy" (as they called it) and local excision of early localized cancers of the vocal cord produced as many cures as laryngectomy, with far less mutilation. This created a sensation and was vigorously contested. For many years it was unpopular in all other countries except England, but before long StClair Thomson, Chevalier Jackson, and the Mayo Clinic published a large series of cases with 75% of five-year survivals. It was always a good operation and still is the best surgical treatment for early lesions. It is a treatment which can be perfectly well carried out in any general hospital by an experienced surgeon. The mortality should be negligible. Nearly all patients have a useful voice afterwards, enabling them to carry on their occupations. A word of caution is necessary. Laryngo-fissure must be undertaken only for the removal of superficial growths which are absolutely localized to the anterior part of the cords. Even a growth which extends into the anterior commissure and affects only a small part of the opposite cord can be successfully removed, but any wide excision of both vocal cords is apt to cause stenosis and the voice may be seriously damaged. As has already been explained, it is sometimes difficult to be certain that the growth is entirely intrinsic, particularly if it is ulcerated and causing loss of movement of the cord. If the cord is completely immobile the disease is probably too advanced for local excision. Undoubtedly, early lesions can now be safely treated by laryngo-fissure.

Radiotherapy : 1. High-voltage X Rays

In 1898 Lewis Jones, using small tubes, began treating cancer with small doses for long periods, up to six months, at St. Bartholomew's Hospital. Since then an enormous amount of money has been invested in equipment which has been improved almost yearly. A colossal amount of research has been done by scientists, and accurate doses can now be given even to deep-seated lesions. More patients have been treated by *x* rays than by any other method. The medical profession and their patients have been told that it is safer than surgery and gives equally good results. As more powerful tubes have become available with an output of millions of volts, and of course costing more and more, the public have been assured that even better results will be obtained.

Unfortunately *x*-ray therapy has been disappointing. Cures are still reported only by special cancer clinics using the latest high potency equipments and by very experienced specialists. Radiotherapists should not treat cancer of the larynx with inferior equipment. They have no hope of good results.

To justify such an assertion it is necessary to analyse the evidence to support it. This can easily be obtained from the general hospitals. There can be little doubt that their *x*-ray treatments for cancer of the larynx have been a failure. It is extremely doubtful whether this bad habit will be cured for a long time : it has obtained such a hold on the public, in spite of its being a long harsh treatment lasting from six to eight weeks. The patient's health often suffers, severe reactions are common, hoarseness and pain persist, the tissues remain swollen, and it may be very difficult to decide whether the growth has been arrested. These signs may be due to perichondritis. Lastly, the skin and deep tissues may be damaged. After a time a new doctor may be consulted and the patient is told that he requires "a few more rays." Repeated ray treatments are often disastrous, and should rarely be given except for palliation of symptoms after recurrence. The following is a typical history :

A patient who complained of persistent hoarseness, probably due to perichondritis, was sent to the country to recuperate. The symptoms worried him, and he consulted a local radiotherapist, who, without a biopsy, advised "a few more *x* rays." A full course was started, but soon caused such inflammation that a tracheotomy became necessary. He suffered agonizing pain and died in six months.

It is only fairly recently that accurate localization of *x* rays has been possible. After a full course there may be severe reaction, and if the skin has been damaged healing may be affected.

A patient who had a recurrence two years after needling was treated with high-voltage *x*-rays and teleradium. Although the skin was scarred laryngectomy was risked. The flaps sloughed and when the wound had recovered a plastic repair with a large pedicle flap was performed, but this also failed to heal. Two further operations were necessary to close the fistula, but he died shortly afterwards of cancer.

Extrinsic cancer is hardly ever cured by *x* rays alone, and never if the lymph nodes are diseased. But the treatment is of the greatest value for the relief of symptoms and for arresting the disease. Occasionally, dramatic results are obtained, and it is difficult to explain why this happens so rarely.

A woman aged 80 had an extensive carcinoma, which obstructed her larynx and required tracheotomy. A full course of deep *x* rays was given by Finzi, and although the lesion did not shrink much it became inactive for four years, when she died of old age. Another cauliflower lesion almost filling the larynx in a man aged 79 entirely disappeared after *x*-ray therapy until his death. A still more remarkable cure should be mentioned. A man of 33 was treated by laryngo-fissure and remained perfectly well for 23 years. He then had a recurrence, and in a short time the growth fungated through the scar and tracheotomy became necessary. After *x*-ray therapy by Finzi in 1932 it disappeared and the patient is still living 20 years later, though a tracheotomy tube is necessary on account of stenosis.

2. Pre-operative Radiotherapy

It is known that even small doses of *x* rays check mitosis temporarily and often shrink new growths to a large extent. In 1925 it was decided to give this treatment a trial : small doses totalling 1,000 to 1,500 r were given on three to five days and needles were inserted a day or two later. In all, 26 patients were treated as shown in Table III.

Table III

	Stage I (6 Cases)	Stage II (17 Cases)	Stage III (3 Cases)	Survival All Stages
3-year survivals ..	5	9	1	58%
5- „ „ ..	5	7	0	46%

3. Teleradium

This seems to be a better treatment than high-voltage therapy for many deep-seated cancers in different parts of the body. For instance it is undoubtedly the best treatment for new growths in the tonsil and post-nasal space. This is fortunate, because surgery is useless. In the larynx it appears to be more successful than *x* rays. It is less harsh, the reactions are milder, and the results are as good as any other treatment. Stanford Cade, to whom I am greatly indebted for advice for so long, has now abandoned other ray treatments, including radium needling, and uses the "bomb" for all stage I early lesions and for some intrinsic stage II growths. The Royal Cancer Hospital (London) has the largest series of laryngeal cancers in England. Lederman uses teleradium exclusively, and laryngectomy only for "failed bomb" cases.

To summarize, the drawback to both *x* rays and teleradium is largely the cost. They require a house to live in, an apparatus which is more expensive each year, and which requires constant repairs—not to mention replacements—and a large and highly trained staff of specialists to run the ship. Obviously it will be impracticable for use in general hospitals, and it is unlikely that there can be more than a few of these units carefully placed in special cancer clinics throughout the country.

The Finzi–Harmer Operation

In 1924 Ledoux, of Brussels, described his "fenestration" operation, which consisted in removal of the cartilage from one side of the larynx and the insertion of short radium needles into the growth. After a visit to Brussels, where we saw some of his patients, it was decided to try the treatment. But to prevent disturbing the growth and risking infection of the wound the needles were placed longitudinally outside the perichondrium covering the lesion. Our second patient, who had an extensive carcinoma and could only whisper owing to fixation of the vocal cord, had been advised to have his larynx removed, but when told that he could be treated by radium first he agreed to take the risk. He was cured by needling and remained well with a strong voice for six years, when he died, of all things, from psittacosis.

If the lesion is not causing severe obstruction to breathing and one vocal cord is moving, intratracheal anaesthesia is safe and preferable to local injections, but, to prevent troublesome bleeding, infiltration of the whole region with procaine and adrenaline is also advisable. The growth itself should not be infiltrated. Two incisions, 2½ in. (6.3 cm.) long, are made, one transversely above the thyroid cartilage with two-thirds of it on the affected side ; the other vertically, over the side of the larynx to the upper rings of the trachea. Two skin flaps are turned laterally to expose the side of the larynx and the infrahyoid muscles. The latter are split from the hyoid bone to the trachea. Bleeding is arrested with coagulating diathermy or ligatures. A mastoid retractor is introduced to separate the muscles and to expose the lateral ala of the thyroid cartilage. The perichondrium is divided with cross cuts and reflected. The lateral ring of the cricoid cartilage is also exposed. With a small curved elevator the perichondrium under the lower margin of the thyroid is separated and a small piece of it is isolated and removed with cutting forceps. This is continued until nothing remains except a narrow frame along the upper and posterior borders. In front, the window should be carried almost to the middle line, leaving the centre keel intact. The upper edge of the cricoid ring is also stripped and notched so that the needles can be pushed under it (Fig. 5). The tissue beneath it is very thin and the dissection must be done with care. On no account must the growth or the larynx be punctured. As already stated, in advanced cases the growth may invade the perichondrium or even the cartilage. This is a serious complication, and unless the lesion is completely encapsulated it can seldom be cured by needling alone. Very rarely there may be upward extension of the growth to the base of the epiglottis, necessitating removal of the greater cornu of the hyoid bone (Fig. 6). The wound must be quite dry before the needles are inserted: each has two silk threads, and each one must be securely fixed with catgut sutures top and bottom.

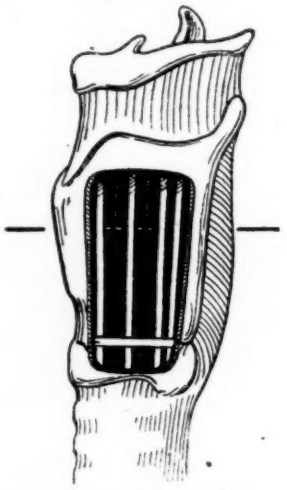


Fig. 5.—The fenestration operation.

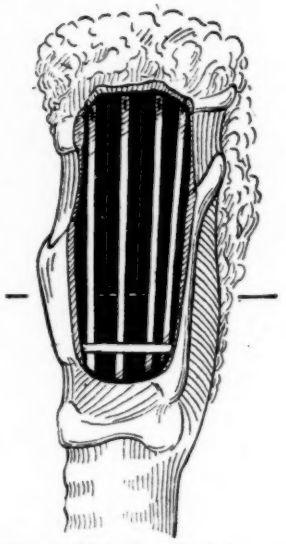


Fig. 6.—The extended fenestration operation.

Unfortunately, for six years it was not realized that the needles are apt to slip out of place and to bunch together : this happened to a distinguished physician who had an extensive bilateral growth for which seven specialists had

advised laryngectomy as the only safe treatment (Fig. 7). He had just heard of radium, and, although at that time only 16 patients had been treated with it, he decided to try it first. A bilateral fenestration was performed. Afterwards he had such violent vomiting that an *x*-ray film was ordered, and this showed that all the needles had slipped and were lying in a bunch by the side of his trachea. The needles were replaced the next day. In three months he resumed full work and was able to lecture with a good voice. He made a daring decision, and is still well after 24 happy years. Because of the possibility of the needles becoming displaced every patient must have a skiagram taken 24 hours after operation.

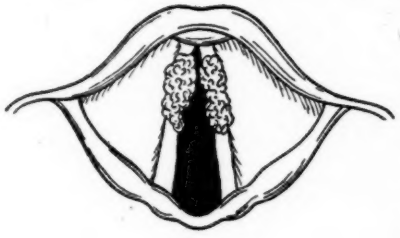


FIG. 7

Bilateral Fenestration.—Lesions of both vocal cords are difficult to cure, and unless the patient is well and has a resonant voice in two or three months laryngectomy should be performed. Fourteen patients had bilateral needling. One had fairly early lesions of the cords and was cured for ten years. He then had a recurrence, but died after laryngectomy. Eleven had extensive lesions which could have been treated only with laryngectomies. Seven died in the first two years. One died of old age in five years. Three are living, for 8, 19, and 24 years, the last the physician mentioned above.

Before closing the wound the cavity should be powdered thickly with sulphanilamide or soaked with 1:1,000 acriflavine solution. The threads are then tied together securely and cut short near the bases of the needles, but leaving one long thread which is fixed to the skin and acts as a guide when they are removed. The infrahyoid muscles are sutured together with catgut over the needles to keep them close to the growth. The transverse skin incision is closed accurately with fine interrupted sutures, which are removed when the wound has healed. In the lower incision, double threads of different colours are inserted, one group cut short to close the wound until the needles are removed, the others kept long for tying afterwards. No drainage is necessary.

Tracheotomy.—From 1924 to 1936 it was difficult to gauge the dose, and later researches showed that this probably varied from 3,000 to 13,000 r in different patients. It is not surprising, therefore, that many of them had severe reactions, with redness, filming, and oedema—particularly of the arytenoid cartilages. For fear of dyspnoea eleven tracheotomies were performed, the tubes being retained until the reaction subsided. Tracheotomy caused serious complications. All the wounds became infected and discharged pus for several weeks. The inflammation sometimes caused necrosis of the cartilages, and healing was naturally very slow. Five other patients required tracheotomy for recurrence. Since 1936 no tracheotomies have been performed after needling. It was found that if a growth was large enough to cause serious obstruction to breathing fenestration was not advisable unless one vocal cord was freely movable. Temporary dyspnoea after the operation can be relieved by retaining the intratracheal tube if necessary for a day or two. If, however, the difficulty of breathing is severe the trachea can be exposed, but not opened unless it is absolutely necessary: only two of the patients required this.

Removal of Needles.—If the wound is not inflamed and there is no swelling in the larynx the needles are usually retained for a week. For removal gas and oxygen or thiopentone can safely be given. The lower wound is opened and the needles are easily removed. Usually there is a small amount of blood-stained serum. The wound should be washed out with acriflavine, 1:1,000, and sutured completely. "Mastisol" is painted on the skin, which is covered with a thin layer of gauze.

Wounds which become seriously infected may be very troublesome. Haemorrhage, sometimes severe, may occur. Extensive sloughing of the tissues may be caused. It is in this type of wound that perichondritis supervenes. Later on it may be followed by necrosis. The treatment of infected wounds is important. All stitches should be removed. The wound should be widely opened, if necessary under an anaesthetic. Debris and sloughs should be removed. The wound should then be packed with gauze soaked in penicillin and sulphanilamide. If the dressing is repeated frequently serious infection is usually controlled in a few days unless there is a communication with the interior of the larynx at the time of the operation which caused the infection. Such wounds may take weeks to heal.

The Dose

A colleague lecturing to students about certain cancers said, "Use radium—plenty of it." This delightful aphorism does not apply to the larynx, which is a difficult customer to please. Great care must be taken not to overdose the patient. From the physical standpoint the great advantage of the radium implant is that irradiation is highly localized, so that there is the minimum interference with unaffected tissues. On the other hand, it is virtually impossible to give a uniform dose to the whole vocal fold by this method. It is true generally, however, that when an irradiated volume is fairly small some non-uniformity in the dose distribution is tolerable provided that the lesion itself receives an adequate dose.

In first treatments, from 1924 to 1936, eight 1-mg. needles were placed touching each other in the window, their ends being tucked under the upper margin of the thyroid above and the cricoid below. It was soon realized, however, that in the middle the dose was too high, causing severe reaction or even necrosis, while at the ends it was inadequate. It varied from 13,000 to 3,000 r. In an ideal arrangement the dose in a week should be about 6,000 r to the anterior half of the cord, but there is a marked fall posteriorly to 3,000 r and also below the free margin of the cord with such short needles of only 16 mm. active length. In spite of this some surprisingly good results were obtained, although these patients must have been overdosed.

Since 1933, when the practice of removing part of the cricoid cartilage was adopted, longer needles have been used though the total amount of radium was approximately as before. As a result, a more uniform distribution of dose is obtained, particularly below the vocal fold. It has been found beneficial to add a transverse 1-mg. needle at the lower ends of the vertical needles in those cases in which the level of the vocal fold is much below the midpoint of the fenestrated area—for example, in many females or in lesions with subglottic extensions.

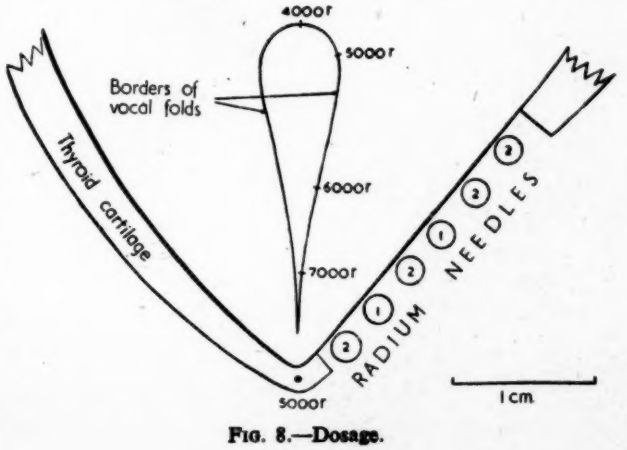


FIG. 8.—Dosage.

For stage I four 2-mg. needles of an active length of 32 mm. are inserted vertically and one or two 1-mg. needles transversely. The screenage of these needles is 0.8 mm. platinum, which is found to produce less local reaction than 0.5 mm.

For stage II rather larger doses are employed. Fig. 8 shows a transverse section of the larynx through the vocal fold for a typical implant of four 2-mg. and two 1-mg. needles (the second and fourth from the front) for a treatment time of one week. With this the anterior half of the vocal fold receives a dose of at least 6,000 r, and nearly all of the vocal fold at least 5,000 r. The fall-off in the dose towards the posterior end of the vocal fold may be partly counteracted by spacing the anterior needles, where the dose is high, rather more widely so that the posterior needles are closer together. In any event, the position of the needles in an implant should be checked the next day by a skiagram and the optimum treatment time for the required dose calculated. More detailed information about the dose distribution was given in 1944 in the *British Journal of Radiology* by Morton, Gray, and Neary, and there is also a good description of the operation in Ralston Paterson's *Treatment of Malignant Disease by Radium and X Rays*. An alternative method, using 1.5-mg. needles of 30 mm. active length, has been used for the vertical implant with a screenage of 0.6 mm., which appears to be nearly as satisfactory as 0.8 mm.

With a bilateral implant both sides contribute equally to the points exactly on the midline. But for a point which is not equidistant from the two implants the contribution from the implant further away is, of course, less than from the near implant. Thus the high local doses in the fenestrated area are not greatly increased by the presence of an implant on the other side. It is therefore difficult to decide, on physical grounds, how much radium is safe in a bilateral implant, since it is not enough to consider the dose at a single point, for no one point is representative for all. Except for very extensive lesions about 12 mg. seems enough.

The Voice

If treatment has been successful the growth soon begins to shrink and inflammation subsides in a few weeks; a fixed vocal cord becomes freely movable again and the resonance of the voice returns. If the disease is not arrested or if it recurs the voice does not improve. Persistent huskiness and swelling may be due to perichondritis or to growth or to both, and a biopsy should be made. Even when the growth is not arrested the report may be negative. In early stages it may be extremely difficult to distinguish these conditions. If the symptoms do not improve within a month or two cancer must be suspected. It is a grave mistake to "wait and see."

Everyone knows that chemical sprays will kill weeds in a lawn and that the grass will recover. When radium is applied to a small localized growth the cancer cells die, the tissues recover, and the voice is normal. The majority of our successes have resulted in a perfect voice. When the voice remains husky it may be owing to damage when making a biopsy. A small notch may prevent perfect apposition of the cords, thus weakening the vibrations. But persistent hoarseness is a serious symptom. The treatment has probably failed, and a "spade"—laryngectomy—is advisable to dig out the weed.

To summarize, fenestration is a slight operation and can safely be performed by surgeons who have a good physicist to advise them about dosage. Not more than 12 needles are needed—a very small outlay. It is a short treatment which is completed in a week. For recurrence, if the lesion is still intrinsic, needling can be repeated. Since using well-filtered needles severe reactions have been rare. Redness, swelling, and filming are slight: oedema of the arytenoid cartilages is hardly ever troublesome. Perichondritis is uncommon and patients do not complain of dysphagia or dyspnoea. Without doubt, some of these patients could have been cured by early laryngectomies. With further experience, it will probably be found that a rule must be observed to remove the larynx unless it is normal in two months. In this series of patients very few laryngectomies were performed—and always too late.

Results

Of the 120 patients needled two went abroad and were lost sight of, as already mentioned. One was treated less than three years ago, so that 117 remain for follow-up analysis for varying periods, as follows:

Treated from 1924 to 1949, 3-year follow-up ..	117
" " " " 1947, 5- " " " ..	111
" " " " 1942, 10- " " " ..	92

Table IV expresses the results in terms of length of survival. The operative mortality must be regarded as high, but should be capable of improvement. Thus between 1924 and 1936 there were 6 deaths in 71 operations (8.5%), while between 1936 and 1951 there were 3 deaths in 49 operations (6.1%). Another feature of interest is that only five patients died of cancer after surviving for three years. There was no evidence, therefore, that metastases were common after needling. Cervical nodes were noted in only six patients, mediastinal deposits in five, and liver secondaries in only one.

TABLE IV.—*Results of the Finzi–Harmer Operation: 1924–1951. 120 Patients Treated (2 Lost)*

Result	Opn. death	Survival in Years: <1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	19	21	24	26	Total
Stage I: Early Intrinsic, 37 Patients																							
Died of cancer or operation ..	1			2								1											4
Died intercurrent disease ..				1	1			1	2	3	2	1			3					1		1	16
Living: years after treatment ..				1	2	2	2	1	1	1	2		1	2		2							17
Survival { At 3 yrs.—32 patients out of 36 treated = 89%																							37
" 5 " —27 " " " 31 " = 87%																							
" 10 " —12 " " " 21 " = 57%																							
Stage II: Advanced Intrinsic, 72 Patients																							
Died of cancer or operation ..	5	9	13	9	6	1	1	2		1			2	1			2	1			1		47
Died intercurrent disease ..						1	1	2	2	2	1		2						1				15
Living: years after treatment ..						2		1	3											1			10
Survival { At 3 yrs.—36 patients out of 72 treated = 50%																							72
" 5 " —26 " " " 71 " = 37%																							
" 10 " —10 " " " 62 " = 16%																							
Stage III: Extrinsic, 9 Patients																							
Died of cancer or operation ..	3		1	4	1																		9
Survival at 3 years.—1 patient out of 9 treated = 11%																						All stages:	118

Stage I : Early Intrinsic (37 patients).—Early lesions were confirmed by removal of the thyroid cartilage in every case. One patient died from the operation, three from cancer (one after 10 years), and sixteen from other causes. Seventeen are still living. Most of the survivors have strong resonant voices. The survival rates are shown in Table IV.

Stage II : Advanced Intrinsic (72 patients).—Usually these were unilateral, extensive, and apparently intrinsic with no enlarged lymph nodes. Twelve were bilateral. Soft tumours, if movable, responded better than the hard nodular ulcerated types. There were five operative deaths from chest infections, which were common when tracheotomies were performed, all of them before the introduction of antibiotics. Forty-two died of cancer, 31 in less than three years, six during the third year, but only five after this critical period. Among these 72 patients 26 survived with their larynges and excellent voices for periods ranging from five to twenty-four years. The survival rates are shown in Table IV.

Stage III : Extrinsic (9 patients).—These patients, who were found to have definite extrinsic lesions without obvious enlargement of cervical nodes, were needled and all of them died within three years. Needling alone has therefore been a failure. But, excepting for two who died of heart failure after operation, seven were temporarily improved for two to three years. Here again, laryngectomies should have been performed while the disease was arrested, and I regret that this was not done.

Summary

Lesions suitable for radium needling are therefore the following :

(1) Early lesions (stage I). Even if the vocal cord is fixed. Lymph nodes are never affected in this group.

(2) Localized lesions in the anterior commissure without involvement of the base of the epiglottis or of the tongue. In this region the dose is always a high one and needling usually succeeds in controlling the disease.

(3) Extensive lesions that appear to be intrinsic (stage II).

(4) Subglottic lesions (really stage III). In a few patients good results have been obtained and there is no risk in trying this treatment first, but laryngectomy should be performed early, in a month or two, if the swelling persists.

(5) Lesions of the false cord and vestibule (stage III). These growths are unusually malignant and difficult to cure. Probably needling plus laryngectomy is the best treatment.

ENVOY

In putting on record the results of 30 years' work with this particular treatment for intrinsic carcinoma of the larynx it would seem to be reasonable to claim that the method has been unduly neglected. I am aware that as good figures have been published claiming that teleradium is superior to interstitial needling for early lesions. I have always maintained that cancer should be treated in special centres by the united efforts of a team of specialists in this disease. Yet there is still a place for simplicity in surgery, and no one can deny that the establishment and maintenance of a teleradium unit is extremely costly. Radiation techniques become increasingly complex and require more and more planning and space and time. The method which we have adopted (and which has been described, possibly a little grudgingly, as "a piece of brilliant empiricism") is relatively cheap and extremely simple in the hands of a competent surgeon. It gives really excellent results if used for the right patient. And it is here, of course, that the clinical experience gained in a long apprenticeship in laryngology counts.

The proof of the pudding is in the eating. I think that this has been a good pudding and that it would be a pity if the recipe were lost.

FOLIC-ACID-EXCRETION STUDIES IN THE INVESTIGATION OF MALIGNANT DISEASE

BY

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When a test dose of 5 mg. of folic acid is injected in a normal individual a significant proportion is promptly excreted in the urine. Most of this excretion occurs within a few hours, but for metabolic studies it is advisable to collect the urine for twenty-four hours after the injection. It has been shown that the urinary excretion of folic acid is diminished in many cases of pernicious anaemia (Bethell *et al.*, 1947 ; Girdwood, 1951, 1953). In a short review of the subject (Girdwood, 1952a) it was suggested that the controls used in the studies of pernicious anaemia patients were unsatisfactory, and that patients with other forms of anaemia should be employed. Accordingly the present investigation was started as a study of folic acid excretion in various types of anaemia. At an early stage it was found (Girdwood, 1952b) that, of eight patients with iron deficiency anaemia, folic-acid excretion was diminished in four. All of these four suffered from carcinoma. It was decided, therefore, to investigate further the urinary folic-acid excretion in patients suffering from malignant disease and from various non-neoplastic conditions. About this time it was reported (Swendseid *et al.*, 1952) that folic-acid excretion was impaired in leukaemia. The patients in the present investigation were all given 5 mg. of folic acid subcutaneously.

Methods and Materials

The estimation of the urinary content of folic acid was carried out microbiologically. Under the conditions of the test the growth of *Streptococcus faecalis* in a suitable medium depends upon the amount of folic acid present in that medium. The growth of the test organism in tubes containing that medium and various dilutions of urine is compared with that in tubes containing the medium and dilutions of a standard solution of folic acid.

Estimations of folic acid were by the method of Teply and Elvehjem (1945), *Str. faecalis R* being used as the test organism. Estimations of citrovorum factor were by a modification of the method of Sauberlich and Baumann (1948) with *Leuconostoc citrovorum* as the test organism. In both instances turbidity readings were carried out in a Spekker photo-electric absorptiometer after incubation at 37° C. for 16 hours. The resting urinary content of folic acid is so small that no correction requires to be made for it in the folic-acid readings. The proportion of folic acid excreted as citrovorum factor is very small, as shown in the accompanying Tables, and the "folic acid" figures include any growth activity due to citrovorum factor. The citrovorum-factor readings have not been corrected for the resting urinary content of citrovorum factor, which on the average is of the order of 1 μg.

The folic acid was given by subcutaneous injection from a tuberculin syringe, and was taken from one or other of two batches of "folvite" that had been tested by us and found to contain 15 mg. of folic acid per ml. Several batches were rejected as they contained more than the stated amount. The volume injected was 0.33 ml.

Twenty-four-hour urine collections were put in brown bottles containing toluene and a phosphate buffer of *p*H 6.8. The greatest possible care was taken to ensure that the urines were total 24-hour specimens. The specimens were kept in a refrigerator at 4° C., and readings were usually

made within three days. All readings were at least in duplicate, usually triplicate. No antibiotics or sulphonamides were given to the patients during the period of the test.

Results

Folic-acid Excretion in Patients Not Suffering from Malignant Disease, Pernicious Anaemia, Intestinal Malabsorption, or Prolonged Infection

The results of the urinary excretion of folic acid in a number of patients with various non-malignant diseases are given in Table I. It will be seen that the only patient in whom the excretion was less than 30% of the dose administered (less than 1.5 mg.) was a man with severe congestive cardiac failure and oedema (Case 43). Two patients, one with a large pleural effusion and the other with massive ascites, are not included; in both instances folic-acid excretion was impaired, but it was possible to show that much of the vitamin was present in the effusion, and that urinary excretion took place over several days. These results suggest that in a patient with normal renal function and without oedema or a large effusion the 24-hour urinary excretion of a 5-mg. dose of folic acid should be greater than 1.5 mg.

It will be seen from Table I that anaemia in itself, even if severe, does not cause an abnormally low folic-acid excretion following a 5-mg. test dose. The same is true of hepatic cirrhosis.

TABLE I.—*Folic-acid Excretion in Patients Without Evidence of Malignant Disease or Prolonged Infection*

Case No.	Sex and Age	Diagnosis	Hb (g.%)	R.B.C. (mil./c.mm.)	Urinary Folic-acid Excretion (mg./24 hrs.)	Urinary C.F. Excretion (μg./24 hrs.)
1	M 35	Normal	15·2	—	3·80	
2	F 34	Agranulocytosis	11·0	5·11	3·75	—
3	M 30	Normal	15·4	—	3·56	—
4	F 34	Erythema nodosum (rheumatic); mitral stenosis	12·3	—	3·55	—
5	M 35	Bleeding duodenal ulcer	13·2	—	3·52	—
6	F 46	Portal cirrhosis; portal hypertension	10·0	3·15	3·41	5·10
7	F 48	Acquired haemolytic anaemia	10·3	3·53	3·32	3·7
8	M 42	Lobar pneumonia	14·8	5·16	3·30	9·6
9	M 77	Neurological features due to vitamin deficiency. Very strict vegetarian	12·3	4·22	3·20	0·83
10	F 32	Brachial neuritis	14·2	—	3·19	—
11	M 49	Bleeding duodenal ulcer	11·6	—	3·19	—
12	F 36	Iron-deficiency anaemia	3·8	2·60	3·16	10·8
13	M 63	Hypertensive cardiac failure	15·4	—	3·16	2·42
14	F 42	Iron-deficiency anaemia	8·1	4·21	3·04	—
15	F 43	" "	7·1	4·98	3·02	4·10
16	F 45	" "	8·6	4·18	2·96	1·55
17	F 49	Portal cirrhosis; portal hypertension	9·0	4·07	2·90	7·4
18	M 51	Gastric ulcer	15·2	—	2·89	—
19	F 34	Peptic ulcer; mitral stenosis	14·0	—	2·89	2·04
20	F 70	Coronary thrombosis; cardiac failure; pulmonary oedema; oesophageal hernia	11·2	5·5	2·80	—
21	F 17	Bronchial asthma	7·3	5·5	2·71	5·4
22	M 57	Polycythaemia	17·3	6·91	2·68	9·0
23	M 52	Gastric ulcer	15·3	—	2·66	—
24	F 66	Iron-deficiency anaemia	7·9	3·65	2·58	—
25	F 16	Thyrotoxicosis	14·8	4·99	2·57	—
26	F 84	Aplastic anaemia	8·0	2·71	2·56	2·0
27	F 72	Portal cirrhosis	13·5	4·40	2·55	3·32
28	M 56	Bleeding duodenal ulcer	9·2	4·72	2·54	1·9
29	F 45	Portal cirrhosis	9·7	3·85	2·50	2·9
30	F 69	Myelosclerosis	8·1	3·15	2·47	3·0
31	F 42	Iron-deficiency anaemia	5·6	4·64	2·42	2·1
32	F 36	Sciatica	11·9	—	2·31	—
33	M 42	Gastric ulcer	14·6	—	2·27	—
34	F 53	Para-oesophageal hernia	8·0	3·13	2·18	6·2
35	F 32	Dyspepsia	13·9	—	2·17	3·1
36	F 18	Bronchial asthma	12·5	—	2·05	—
37	F 48	Gastric neurosis	15·3	5·01	2·02	1·38
38	F 46	Iron-deficiency anaemia	8·1	4·67	1·93	7·36
39	F 42	Sciatica	14·2	—	1·73	—
40	F 66	Chronic alcoholic; bronchopneumonia; malnutrition	15·0	—	1·73	—
41	F 68	Malnutrition	9·3	3·6	1·52	1·47
42	F 84	"	4·0	3·1	1·52	2·8
43	M 66	Hypertensive cardiac failure with oedema	15·2	—	0·79	1·60

C.F.=Citrovorum factor

Folic-acid Excretion in Patients Suffering from Malignant Disease and Allied Conditions

In Table II there are given the urinary folic-acid excretion results in a number of persons suspected of having malignant disease (including leukaemia and the reticuloses) or found as a result of hospital investigation to be so afflicted. The Table is constructed so as to include the provisional diagnosis when the patient was first seen in connexion with the present investigation. Thus in many instances it was not known whether or not malignancy was present, and it will be seen that in some cases it was fortunately possible to show that no neoplastic disease existed. In the cases included in this Table the final diagnosis had been definitely established, in many instances by biopsy or laparotomy. Most of the patients included in Table II had had no therapy, but a few had been treated by *x* rays or other means several months before the present investigation.

It will be seen from Table II that a *normal* folic-acid excretion (1.5 mg. or less after the subcutaneous injection of 5 mg.) is of no help in excluding the presence of malignancy. Fourteen patients with carcinoma, leukaemia, lymphadenoma, or some other form of reticulosis had a normal folic-acid excretion. It is true that in most of these cases the general condition was good and there was little evidence of spread, but this was not so in Cases 53, 64, 66, and 73. Case 63 suffered from weakness and pyrexia, but no abnormality was found on physical examination. The diagnosis of lymphadenoma at the time of the folic-acid test was made only by exclusion and treatment with nitrogen mustard was begun. Despite the satisfactory folic-acid test, the diagnosis of lymphadenoma was confirmed at necropsy only three months later. Case 51 felt so well despite the abnormal blood picture that no treatment was given.

Inspection of the records of cases in Table II who excreted less than 1.5 mg. of folic acid shows that all of them suffered from malignant disease. In some instances the folic-acid-excretion results were available some time before the presence of malignancy was established by *x*-ray films, biopsy, or laparotomy. Obvious weight loss was not invariably present in patients with a positive test. It will be seen, too, that there was no correlation between the sedimentation rate or the degree of anaemia and the result of the folic-acid-excretion test in either malignant or non-malignant cases.

Folic-acid Excretion in Chronic Infection

There are occasions on which it would be helpful to have a test to determine whether a patient suffers from chronic infection or from malignancy. For this reason a separate table (Table III) has been constructed to include untreated patients with chronic infections and collagen diseases. In all the cases of pulmonary tuberculosis the disease was extensive, but except in Cases 106 and 115 the general condition under a sanatorium regime was good.

Case 118 illustrates most clearly that prolonged generalized bacterial infection can give a diminished output of folic acid after a test dose. No treatment had been given for a year.

In Case 115 the possibility that amyloid tissue has an affinity for folic acid would require consideration.

It is possible that the diagnosis in Case 117 was incorrect, as there was an increase in plasma cells in the marrow, and the symptoms and fever did not respond to salicylates.

Case 114 is of interest in that the patient's general condition was good, and the only obvious abnormality was splenic enlargement. Nevertheless the test was positive.

Four patients with pyrexia, the cause of which is not yet certain, are included to show that prolonged fever will not itself necessarily lead to a diminished excretion of folic acid. In this respect Case 99 is of interest in that quite high fever—rising to 103° F. (39.4° C.)—has been present intermittently for 18 months without evidence of general deterioration. The diagnosis of Case 108 is uncertain, but,

although emaciation was severe, folic-acid excretion was normal. Case 116 (lupus erythematosus disseminatus) was also much wasted, and, although cortisone therapy led to marked clinical improvement, the folic-acid excretion remained abnormal in this patient.

Folic-acid Excretion in Megaloblastic Anaemia

This is the subject of other communications (Girdwood, 1951, 1953), and hence the only information required here is a summary of the findings in 20 cases of untreated pernicious anaemia, 2 cases of intestinal malabsorption that had

TABLE II.—*Folic-acid Excretion in Patients Suspected of Having Malignant Disease*

Case No.	Sex and Age	Suspected Malignancy or Diagnosis on Admission	Hb (g.%)	R.B.C. (mil/c.mm.)	E.S.R. (mm./hr.) (Westergren)	Final Diagnosis	Urinary Folic-acid Excretion (mg./24 hrs.)	Urinary C.F. Excretion (μg./24 hrs.)	Remarks
44	M 64	Gastric carcinoma (*x*-ray confirmation)	10·0	3·82	45	Gastric ulcer (non-malignant) at operation	4·05	—	
45	F 48	Carcinomatosis	13·6	—	45	Carcinoma of cervix. No evidence of secondaries	3·7	—	Good general condition
46	F 52	,, ...	14·9	—	3	Brain-stem thrombosis	3·7	1·87	
47	F 50	Gastric carcinoma	12·2	5·26	50	Gastric ulcer (non-malignant) at operation	3·7	—	
48	F 51	Hepatic carcinoma ..	14·0	—	90	Rheumatoid arthritis	3·54	—	
49	M 43	Lymphadenoma ..	16·0	5·31	—	Lymphadenitis	3·50	—	
50	F 43	Plasma-cell tumour of breast (biopsy before admission)	14·2	4·92	3	Plasma-cell tumour of breast	3·48	4·7	Good general condition
51	M 66	Chronic lymphatic leukaemia	14·8	—	—	Chronic lymphatic leukaemia	3·46	10·3	Feels quite fit. No glandular, hepatic, or splenic enlargement. W.B.C. 112,800. No treatment given
52	M 60	Carcinoma of liver ..	14·0	—	38	Carcinoma of gall-bladder	3·33	2·47	
53	F 67	Bronchial carcinoma ..	6·0	4·3	90	Pulmonary tuberculosis; carcinomatous glands in neck; primary uncertain	3·19	5·5	
54	F 68	Carcinomatosis; myxoedema	10·0	2·89	112	Spondylitis; myxoedema	3·16	0·63	
55	F 44	Gastric carcinoma ..	11·5	5·5	8	Hiatus hernia	3·10	—	
56	F 63	Suspected malignancy ..	11·8	4·08	110	Coronary thrombosis	3·06	—	Weakness and raised E.S.R.
57	M 58	,, ,, ..	12·3	4·8	14	Anxiety state	3·02	—	Tiredness and weight loss
58	F 23	Lymphadenoma ..	13·6	—	24	Pulmonary and glandular tuberculosis	2·88	5·1	
59	F 70	Neck swelling; diabetes	15·6	5·62	5	Lymphosarcoma; diabetes	2·72	16·3	Liver and spleen not enlarged; good general condition
60	M 74	Carcinoma of gall-bladder	13·2	—	12	Gastric carcinoma: local spread to liver	2·6	3·1	Good general condition
61	M 45	Lymphadenoma ..	15·2	—	28	Lymphadenitis	2·6	8·47	
62	F 73	Bronchial carcinoma; rheumatoid arthritis	13·0	—	62	Bronchial carcinoma ; rheumatoid arthritis	2·50	—	Slowly progressive over years
63	M 51	Lymphadenoma ..	8·7	3·21	127	Lymphadenoma	2·42	—	Pyrexia. No enlargement of glands or organs; died 3 months later
64	F 42	Acute lymphatic leukaemia	13·3	4·98	32	Acute lymphatic leukaemia	2·40	1·58	Enlarged liver, spleen, glands. Died soon after. W.B.C. 26,200
65	F 60	Suspected malignancy	14·1	—	48	No abnormality found	2·35	—	Weight loss; epigastric discomfort
66	M 56	Bronchial carcinoma ..	14·0	—	5	Bronchial carcinoma with metastases	2·27	3·5	
67	F 74	Carcinoma of caecum ..	—	—	—	Carcinoma of caecum (localized)	2·24	—	
68	F 50	Carcinoma of liver ..	12·3	—	—	Infective hepatitis	2·04	3·98	Serum bilirubin 13 mg./100 ml.
69	F 77	Carcinomatosis	8·8	2·47	70	Pelvic abscess	2·0	10·2	
70	F 46	Intestinal reticulosis ..	14·8	4·86	9	Intestinal reticulosis	1·97	4·4	Biopsy diagnosis. No evidence in other organs
71	F 56	Carcinoma small intestine	12·2	—	80	Adhesions	1·95	0·76	
72	M 63	Hepatic carcinoma ..	15·2	4·83	2	No abnormality found	1·90	2·70	
73	M 55	Aleukaemic lymphatic leukaemia	9·8	3·4	65	Aleukaemic lymphatic leukaemia	1·75	2·85	W.B.C. 5,000. Glands, liver, spleen normal. Died a month later
74	M 73	Glandular enlargement..	11·0	4·3	100	Reticulosis	1·20	—	Very little weight loss
75	F 41	Pernicious anaemia refractory to vitamin B_{12}	9·3	3·04		Pernicious anaemia; gastric carcinoma: metastases	1·16	—	
76	F 76	Iron-deficiency anaemia	6·2	3·03	47	Inoperable carcinoma of transverse colon	1·04	—	No weight loss
77	M 45	Lymphadenoma ..	8·6	—	125	Renal carcinoma	0·98	8·65	Normal renal function. No weight loss
78	M 71	Follicular reticulosis (biopsy diagnosis)	12·7	4·35	—	Follicular reticulosis	0·97	4·57	
79	F 62	Refractory iron-deficiency anaemia	5·4	2·9	50	Carcinoma of jejunum	0·796	4·61	
80	M 52	Glandular enlargement..	14·9	4·98	—	Follicular reticulosis	0·762	—	
81	M 49	Lymphadenoma ..	12·0	4·25	—	Lymphadenoma	0·75	3·6	No weight loss
82	M 62	Iron-deficiency anaemia	4·6	2·97	6	Carcinoma of stomach and liver	0·71	—	
83	M 63	Same patient as Case 82 a year later	9·0		47	,, ,, ,,	0·112	1·64	No clinical deterioration, but mass larger
84	M 32	Anaemia	7·6	2·31	—	Acute lymphatic leukaemia	0·715	3·5	Three weeks' illness
85	M 69	Jaundice	11·3	—	50	Carcinoma of liver	0·601	—	Serum bilirubin 120 mg./100 ml.
86	F 46	Uterine carcinoma; secondaries	3·5	1·67	125	Uterine carcinoma; secondaries	0·472	2·29	
87	M 48	Lymphadenoma ..	14·2	5·19	60	Lymphadenoma	0·46	12·8	
88	F 39	Pain in back—for investigation	9·0	3·1	125	Multiple myeloma	0·343	3·38	No weight loss
89	F 59	Chronic myeloid leukaemia	8·4	3·28	25	Chronic myeloid leukaemia	0·325	6·55	W.B.C. 384,000
90	F 22	Lymphadenoma ..	7·5	2·4	110	Lymphadenoma	0·221	—	Very little weight loss
91	M 34	Glandular enlargement..	14·8	—	47	,,	0·142	5·75	
92	F 32	Multiple myeloma ..	12·3	—	57	Multiple myeloma	0·134	2·91	
93	M 37	Lymphadenoma ..	8·5	3·08	—	Lymphadenoma	0·133	—	
94	F 42	Emaciation	10·2	3·55	120	Carcinomatosis	0·100	8·4	
95	F 66	Anaemia	6·6	2·80	8	Lymphosarcoma	0·084	3·35	No hepatic or glandular enlargement. Spleen just palpable. No weight loss
96	M 66	Chronic lymphatic leukaemia and cardiac failure	11·1	3·44	—	Chronic lymphatic leukaemia and cardiac failure	Negligible	Negligible	

TABLE III.—*Folic-acid Excretion in Patients with Chronic Infections or Associated Conditions*

Case No.	Sex and Age	Diagnosis	Hb (g.%)	R.B.C. (mil./c.mm.)	E.S.R. (mm./hr.)	Years of Illness	Urinary Folic-acid Excretion (mg./24 hrs.)	Urinary C.F. Excretion (μg./24 hrs.)	Remarks
97	F 27	Rheumatoid arthritis ..	8·6	—	60	6/12	4·23	—	
98	M 23	Pulmonary tuberculosis		—	5	6	3·49	—	Extensive bilateral
99	F 26	P.U.O.	12·5	4·88	5	1½	3·48	5·73	Temperature to 103° F. (39·4° C.), good general condition
100	M 37	Pulmonary tuberculosis		—	52	2	3·34	—	Bilateral
101	F 23	P.U.O.	12·4	4·14	18	3/12	3·23	6·5	Temperature to 99·5° F. (37·5° C.)
102	M 47	Pulmonary tuberculosis	—	—	2	3	3·01	—	Large cavity
103	F 52	Chronic bronchitis with acute recurrence	14·0	—	100	20	2·98	—	
104	M 62	Pulmonary tuberculosis	—	—	35	1½	2·62	—	Bilateral
105	M 53	" "	—	—	47	2	2·59	—	"
106	M 67	" "	14·2	—	26	Many	2·43	4·07	Extensive unilateral
107	F 21	Undulant fever ..	15·2	—	12	2/12	2·38	11·2	
108	F 43	P.U.O.			22	1½	2·38	—	Lost 3 st. (19 kg.)
109	F 63	Rheumatoid arthritis ..	9·9	3·37	5	3	2·30	2·79	
110	F 70	Severe chronic bronchitis with heart failure	13·0	4·5	40	Many	2·2	—	Much wasted
111	M 48	Pulmonary tuberculosis	—	—	40	1	2·14	—	Extensive bilateral
112	M 52	P.U.O.	13·4	5·82	130	4/12	1·79	—	Temperature to 101° F. (38.3° C.)
113	F 53	Chronic pneumonia with eosinophilia	11·0	3·86	74	1½	1·74	—	
114	M 46	Sarcoidosis	14·6	5·01	—	Recent	1·15	2·15	Splenic enlargement only. Diagnosis after splenectomy
115	F 45	Pulmonary tuberculosis amyloid liver	—	—	55	13	1·14	6·13	
116	F 50	Lupus erythematosus disseminatus	7·4	3·58	110	2	0·95	—	
117	F 50	Rheumatoid arthritis ..	14·8	—	35	2/12	0·825	—	Did not respond to salicylates
118	M 26	Subacute bacterial endocarditis (untreated)	11·0	3·63	76	1	0·14	—	

not received folic acid, vitamin B_{12}, or citrovorum factor, 7 cases of megaloblastic anaemia of pregnancy, and 1 case of idiopathic refractory megaloblastic anaemia.

TABLE IV.—*Folic-acid Excretion in Megaloblastic Anaemia (Untreated)*

	No. of Cases	Folic-acid Excretion (mg.) Following a 5-mg. Test Dose given Subcutaneously
Pernicious anaemia	20	0·066–3·08 (mean 1·55)
Intestinal malabsorption	2	0·126, 0·299
Pregnancy (megaloblasts, not transitional erythroblasts, present) ..	4	1·33, 1·50, 2·37, 2·64
	3*	1·58, 1·75, 3·84
Idiopathic refractory megaloblastic anaemia	1	1·92

* Received 15 mg. of folic acid by injection.

In all these patients the marrow was frankly megaloblastic: examples where transitional erythroblasts were found are recorded separately (Girdwood, 1953).

It will be noted from Table IV that in megaloblastic anaemia of pregnancy folic-acid excretion may be normal. Of the 20 pernicious-anaemia patients, 9 had an excretion of less than 1.5 mg.

Discussion

These results suggest that the folic-acid excretion test may have a limited place in the investigation of puzzling cases. Many more cases must be studied before we can say to what extent the test is of value in differentiating between such conditions as aplastic anaemia and aleukaemic leukaemia or simple iron-deficiency anaemia and iron-deficiency anaemia associated with advanced malignant disease. It is obvious that a "negative" test (normal excretion) is of no assistance to the clinician in the diagnosis of malignancy, since in 14 cases a normal excretion of folic acid was found. On the other hand, where there is no evidence of intestinal malabsorption, prolonged fever, megaloblastic anaemia, a large effusion or generalized oedema, and where renal function is not impaired, a "positive test" (an excretion of less than 30% of a 5-mg. test dose) would appear to suggest the presence of malignancy. Further investigations may show additional exceptions to this generalization. It is important that an exact dosage of folic acid should be given, and the urine collection must be complete. We have found that a repetition of the test dose may give a less abnormal finding on the second occasion, possibly because the first 5 mg. of folic acid partially corrects the folic-acid deficiency in the tissues.

It is not certain what a diminished urinary excretion of folic acid indicates. In nutritional megaloblastic anaemia, and in untreated cases of intestinal malabsorption, the presence of megaloblasts in the marrow is taken to indicate deficiency of folic acid or of vitamin B_{12}. In untreated pernicious anaemia, in which the primary deficiency is believed to be of vitamin B_{12}, folic-acid excretion following a test dose is frequently low, but can be normal. Moreover, transitional erythroblasts rather than true megaloblasts may be found in association with either a normal or an abnormal output of folic acid. The excretion in megaloblastic anaemia of pregnancy may be normal or abnormal, and this is discussed elsewhere (Girdwood, 1953). In malignant disease the amount of the test dose of folic acid excreted may be much diminished, but megaloblasts are only very rarely found in the marrow. They were not seen in any of the cases reported here.

One possible explanation both of the absence of megaloblasts and of the low urinary excretion of folic acid would be that the tumour tissue competes with the host for folic acid or its derivatives, but not to the extent of depriving the red-cell precursors of enough folic acid for maturation along normoblastic lines. Such a possibility is understandable where there is widespread malignancy as in leukaemia (for example, Case 84, in which the illness had been of only three weeks' duration and there would hardly be time for any other mechanism to play a part). The occurrence of megaloblastosis cannot be related directly to the degree of impairment of urinary folic-acid excretion, since the mechanism of production of megaloblastic change in the marrow varies in different conditions. It is possible that where the primary fault is virtual absence of folic acid or associated substances from the diet, or malabsorption of the folic-acid group of vitamins, a greatly diminished urinary output of administered folic acid will be associated with megaloblastosis; but we have seen that where the primary fault is the absence of vitamin B_{12}, or where there seems to be mal-utilization of folic acid in the body (for example, pregnancy megaloblastic anaemia) this relationship does not necessarily hold.

Other modes of production of the apparent folic-acid deficiency in cases of malignant disease that merit consideration are deficient intake due to anorexia with resulting primary malnutrition, and diminished absorption produced by widespread metastases or some other means.

It seems unlikely that either of these mechanisms could operate without significant weight loss occurring, and there was little or no weight loss in Cases 74, 76, 77, 81, 84, 88, 90, 95, and 114. Moreover, in Cases 77 and 114 there was no evidence at operation of any cause for intestinal malabsorption. This was true also at post-mortem examination in Cases 88 and 95.

In contrast, there was very severe primary malnutrition of many years' duration in Cases 40, 41, and 42, as established by a detailed dietetic investigation. An important source of calories for Case 40 was whisky. Case 41 weighed only 4 st. 12 lb. (30.8 kg.): a fat-balance test in this patient revealed normal fat absorption. A post-mortem examination of Case 42 revealed no abnormality other than generalized wasting.

Nevertheless these patients, while excreting less of the administered folic acid than did most of the other control cases, were able to excrete 1.5 mg. or more.

It is, of course, possible that several factors operate to give a diminished folic-acid excretion in some patients with malignant disease. Thus it would be reasonable to assume that intestinal malabsorption was an important cause in Case 79. Recently a folic-acid-absorption test has been devised for measurement of absorption of folic acid from the alimentary tract (Girdwood, 1953), and it may be that the application of this test to cases similar to those in Table II will be of value.

The data given do not indicate whether the result of the folic-acid-excretion test is of help in assessing the prognosis or of value in considering the best method of treatment to adopt, especially in patients with leukaemia or some form of reticulosis. Case 63 had a normal folic-acid excretion and died within three months. Case 87 had a very abnormal excretion, but is alive and well following *x*-ray therapy.

Summary

A test dose of 5 mg. of folic acid was given subcutaneously to 148 patients. The urinary excretion of folic acid usually exceeds 30% of the test dose, and an excretion of less than 1.5 mg. is recorded as a "positive" test.

The test may be positive in megaloblastic anaemia, but there is no evidence that anaemia in itself gives a diminished excretion.

Where renal function is good and the patient does not suffer from megaloblastic anaemia, intestinal malabsorption, generalized oedema, a large effusion, or severe infection of long duration, a positive test is likely to indicate the presence of advanced malignant disease. It is, however, possible to have advanced malignancy with a negative folic-acid test.

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THE PREVALENCE OF FOOT DEFECTS AMONG WARTIME RECRUITS

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There is a general, if unconfirmed, impression that foot defects are common, painful, and incapacitating enough to justify more attention than they have hitherto received from epidemiologists. A recent survey in Luton has indicated the number of persons who themselves complain of foot trouble (Dykes, Grundy, and Lee, 1952), but assessments of incidence based on clinical observations are mainly confined to children (Emslie, 1939; Wilkins, 1941), young women (Alford and Gorrie, 1952), and aged persons (Sheldon, 1948). In the present investigation the registers of Civilian Medical Boards, which are more fully described elsewhere (Martin, 1949; Clements and Pickett, 1952) have been used to obtain an estimate of the prevalence of foot defects in men of working age and, where possible, to identify predisposing factors.

The registers used in the present survey relate to men who were called up in 1941 and examined in Leicester. According to the official instructions circulated to the Medical Boards, "special attention should always be drawn to the defects which may cause a man to be classified in one of the lower grades of fitness for military service, or which may influence decision on possible claims for pension in the future: these should be described as in a clinical report." The instructions stress the importance of recording all types of foot defect and state that a detailed examination of the feet may be omitted only if a man is so severely disabled in other respects as to be totally unfit for military service. There were 358 such cases in the Leicester records. After the exclusion of these, and of a further 93 over 45 years of age, there remained 22,843 men between the ages of 17 and 44, of whom 3,287 (14.4%) shared 4,160 foot defects.

Age Distribution and Interrelation of Foot Defects

The distribution of foot defects by age and diagnosis is shown in Table I. The two categories of flat-foot distinguish cases in which the arch could be restored by standing on tip-toe (mobile, or A cases), and cases in which the

TABLE I.—*Foot Defects Recorded at Specified Ages: Men Examined at Leicester in 1941*

Defect	Cases per 1,000 Examinees Aged						Total No. of Cases
	17–19	20–24	25–29	30–34	35–39	40–44	
Of longitudinal arch:							
Flat-foot (A cases)	38·9	38·6	36·7	39·0	36·6	45·6	880
,, (B ,,)	8·5	11·6	20·4	24·6	34·8	38·2	502
Pes cavus	5·2	7·9	10·7	11·2	14·4	12·7	233
Of forefoot:							
Hammer-toe ..	20·5	32·5	44·1	48·4	61·9	67·1	1,003
Hallux valgus ..	13·9	15·1	26·0	33·5	40·0	46·9	640
,, rigidus ..	2·3	1·8	7·4	7·3	8·4	6·0	126
Overlapping toes ..	12·0	12·7	17·2	21·1	22·7	20·1	405
Other:							
Callosities	5·0	5·5	10·7	21·1	25·8	26·2	356
Miscellaneous ..	0·8	0·5	0·9	1·0	0·4	0·0	15
No. of examinees ..	4,835	3,786	2,153	5,082	5,496	1,491	22,843

longitudinal arch had permanently disappeared (rigid, or B cases).* The category "miscellaneous" includes deformed nails (5), extra toes (3), skin pedicles (2), webbed toes (1), and four undiagnosed cases.

According to Table I the A cases of flat-foot showed a fairly level age incidence, but the B cases increased steadily with age to become four times as common in the early forties as in the late 'teens. In theory this discrepancy can be accounted for in several ways, but the most likely explanation (which assumes that the A cases represent a stage between normality and total extinction of the longitudinal arch) is that new cases were occurring between the ages of 17 and 44 at roughly the same rate as established cases were progressing to an irreversible stage. If, however, the A and B cases of flat-foot are two distinct clinical entities then the figures in Table I can be explained only by assuming that (1) mobile as well as rigid flat-foot is an irreversible condition; (2) regularly throughout the age group 17 to 44 years new cases of rigid flat-foot continued to develop *de novo*; and (3) virtually all the cases of mobile flat-foot were manifest before the age of 17.

Table I also shows the incidence of metatarsal and related defects at various ages. The two most common conditions in this group show a rising age incidence, and by the early forties nearly 7% of men had hammer-toes, and nearly 5% had hallux valgus. A similar though less noticeable increase with age is seen in the case of callosities and overlapping toes, but the incidence of hallux rigidus shows little variation within the age range 17–44. There was also a distinct tendency for foot defects, especially when severe, to occur together. A measure of this tendency is shown in Table II,

TABLE II.—*Frequency of Multiple Foot Defects*

r	No. of Men with *r* Defects	Expected No. of Men with *r* Defects, on the Assumption that Defects Occur Independently
0	19,564	18,970
1	2,554	3,594
2	584	267
3	129	}
4	11	} 12
More than 4	1	}
All	22,843	22,843

which gives the actual number of men having 0, 1, 2, 3, 4, and more than 4 defects and the numbers to have been expected if each defect had occurred independently.

The expected figures were obtained by multiplying the appropriate proportions and summing when necessary. For example, the expected proportion with exactly one defect was $\sum_i \left\{ \frac{p_i}{1-p_i} \left[\prod_i (1-p_i) \right] \right\}$ in which p_i stands for the proportion of men with the ith defect. In this calculation both categories of flat-foot are, of course, treated as one defect, since by definition they cannot occur together.

It will be seen that isolated defects occurred with less than three-quarters, pairs of defects with over twice, and three or more defects with nearly twelve times their expected frequency. The following list shows the extent to which particular defects tended to be associated, the figure beside each defect being the ratio of the number of times it was found in conjunction with other defects to the expected number, in the sense defined above: callosities, 4.75; flat-foot (B cases), 3.59; hallux valgus, 3.54; hallux rigidus, 3.10; overlapping toes, 3.05; hammer-toe, 2.80; pes cavus, 2.76; flat-foot (A cases), 0.64. The position of callosities at the head of the list reminds us that these painful skin lesions are apt to accompany every variety of bony displacement. The list also shows that mobile flat-foot is rarely and rigid flat-foot commonly found in association with other deformities. This suggests that by the time other lesions have developed in flat-footed persons the longitudinal arch has usually disappeared.

The analysis of multiple defects was carried one stage further by calculating "association" ratios for specific pairing of defects. The two most frequent pairings were hammer-toe and callosities (121 times) and hallux valgus and hammer-toe (104 times), but for several other well-known combinations the excess relative to the "expected" number of cases was even greater. Thus hallux valgus and overlapping toes were eight times, hallux rigidus and flat-foot seven times, and pes cavus and hammer-toe four times, as common as they would have been if they were independent lesions.

The tendency for bony deformities of the foot to be found in association with diseases which affect other parts of the skeleton was also studied and foot defects were found to be especially common in persons who had had the paralytic form of poliomyelitis. There were also significant associations for lower limb injuries, curvature of the spine, rheumatoid arthritis, and for a mixed group of skeletal conditions mainly composed of operations on the lower limb and undiagnosed wasting of leg muscles.

Relation of Foot Defects to Body Size and Build

According to Lake (1943) the human foot is still imperfectly adapted to the extra strain imposed upon it by the upright posture. Since this strain is related to body build it was thought worth while to examine the association between overt foot defects and certain measurements recorded at the time of the medical board.

In Table III the number of men (×100) with foot defects who fall into eight weight groups has been compared with the number to have been expected if the risk of foot troubles were independent of weight. The corresponding analysis for height is shown in Table IV. In both tables the age distribution of the different groups has been taken into consideration. The numbers on which the ratios are based have also been subjected to a statistical test which measures the likelihood of obtaining so large a departure from expectation as a result of chance fluctuations only. The results of these χ^2 tests are shown in the right-hand column of the table.

For foot defects as a whole (bottom line of Table III) there was no perceptible association with body weight, but a few specific conditions revealed statistically significant departures from expectation. The most definite of these associations were the exceptionally high ratios for rigid flat-foot, pes cavus, and overlapping toes in men weighing less than 110 lb. (49.9 kg.). The findings for A cases of flat-foot were inconclusive, but the highest ratio was at the heavy end of the weight scale, whereas for B cases it was at the lowest end.

For all types of foot defect taken together the association with height was much stronger than that with weight, and there were also significant associations for several individual lesions (see Table IV). Once again, however, the findings were not straightforward. Thus, overlapping toes were less common among medium-sized men than among either tall or short men; both categories of flat-foot had a maximum incidence in short men, and all the metatarsal deformities gave high ratios at or near the top of the height scale. In the extreme case of hammer-toe the risk for men of 70 in. (178 cm.) or taller was over twice as great as for men of 64 in. (162.5 cm.) or shorter. There are no measurements of foot length in civilian medical board records, but Morant and Gilson (1945), who studied men in the Royal Air Force, found that the coefficients of correlation between foot length and height, and foot length and weight, were +0.700 and +0.557 respectively. This may account for the departures from level incidence associated with variations in height being greater than those associated with weight.

*According to the official instructions, all A cases were automatically placed in the top fitness category (Medical Grade I) and B cases in Medical Grade IIa (feet), but in the presence of more disabling conditions the medical grade no longer serves to distinguish the two groups. These cases had to be "placed" at the time of coding and the convention was adopted that, in the absence of fuller clinical descriptions, all cases of "mild" or "slight" flat-foot should be coded A and all cases of "severe" or "disabling" flat-foot coded B.

TABLE III.—*Relation Between Body Weight and Incidence of Foot Defects. Standardized for Age (Standard Incidence=100)*

Foot Defect	Weight (lb.)										Probability (P) that the Observed Departures from Standard Incidence could have Arisen by Chance
	<100	<110	<120	<130	<140	<150	<160	<170	<190	190+	
Flat-foot (A cases)	76		100	108	102	86	111	100	112		0·20>P>0·10
,, (B ,,)	151		105	88	88	109	76	106	138		0·01>P>0·001
Pes cavus	160		96	85	123	87	80				0·05>P>0·02
Hammer-toe	89		91	98	105	105	99	133	84		0·30>P>0·20
Hallux valgus	118		107	104	95	97	100	89	77		0·80>P>0·70
,, rigidus		120		114	89	69	101				0·50>P>0·30
Overlapping toes	143		115	104	102	176	86	82			0·10>P>0·05
Callosities		98		96	107	99	81	120			0·80>P>0·70
One or more of the above	110	104	103	99	99	95	98	110	105	102	1·00>P>0·90

TABLE IV.—*Relation Between Standing Height and Incidence of Foot Defects. Standardized for Age (Standard Incidence=100)*

Foot Defect	Height (in.)							Probability (P) that Observed Departures from Standard Incidence could have Arisen by Chance
	<62	<64	<66	<68	<70	<72	72+	
Flat-foot (A cases)	145	110	102	102	88	102	92	0·20>P>0·10
,, (B ,,)	123		103	93	96	98		0·50>P>0·30
Pes cavus	83		105	91	96	134		0·30>P>0·20
Hammer-toe	62		79	86	128	154	135	0·001>P
Hallux valgus	97		89	99	101	112	148	0·20>P>0·10
,, rigidus		106		98		96		0·90>P>0·80
Overlapping toes	113		96	86	97	130		0·10>P>0·05
Callosities	68		94	87	115	144		0·01>P>0·001
One or more of the above	106	96	94	95	102	118	121	0·01>P>0·001

Considering the close association between weight and height (the coefficient of correlation for the present set of records was +0.725) there were remarkably few examples of contrasts between light and heavy men appearing again as contrasts between short and tall men. On the other hand, there were several examples of the same risks for short men and heavy men—for example, flat-foot—and for tall men and light men—for example, hammer-toe. It is clear, therefore, that certain foot defects are as closely related to general build as to absolute size.

An attempt was made to measure the relationship between foot defects and body shape, but only three measurements were available for the purpose—namely, height, weight, and chest circumference. However, Burt and Banks (1947) have demonstrated, by means of a factor analysis of nine sets of measurements taken from Royal Air Force recruits, that it is possible to discriminate between stocky and slender types on the basis of height and weight alone. The particular combination of height and weight used in this study (height in inches divided by the cube root of the weight in pounds) has a minimum value for a perfectly spherical body, and increases with increasing linearity of build. In adult males the normal range of variation of this index is from 11½ to 14½. Since the index tends to fall with age, the incidence ratios plotted in the Chart have been standardized for age in the same way as the separate ratios for height and weight. The diagram traces the relationship between the body-build index and the incidence of two groups of foot defect—namely, tarsal (that is, both grades of flat-foot) and metatarsal (that is, hallux valgus, hallux ridigus, overlapping toes, and hammer-toe, either alone or in combination). The figure shows that for stocky men, with low values of the body-build index, flat-foot occurred in excess. It is possible, therefore, that overweight, or some associated condition, predisposes to this type of foot defect. The incidence of metatarsal defects, however, rose continuously with increasing linearity of build, and the risk appeared to double within the observed range of the index. For these cases, therefore, it is more reasonable to look for causes associated with underweight or slender build.

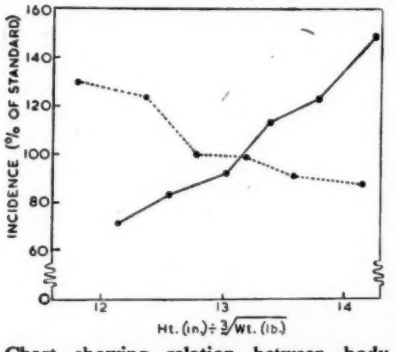

Chart showing relation between body shape and incidence of foot defects, standardized for age. (Standard incidence=100.) Probability that observed departures from standard incidence could have arisen by chance: Flat-foot (broken line), 0.01>P>0.001; forefoot defects (continuous line), P<0.001.

Relation of Foot Ailments to Economic Circumstances and Occupation

According to the Foot Health Educational Bureau (1949) "Exact figures are hard to come by, but, though as yet we have no unselected random sample of foot conditions among adult groups in Great Britain, it is probably correct to say that ailments of the feet . . . are distributed irrespective of income level." From an analysis of the civilian medical board records, however, it appears that this statement is almost certainly incorrect (see Table V).

TABLE V.—*Relation Between Social Class and Incidence of Foot Defects. Standardized for Age (Standard Incidence=100)*

Foot Defect	Social Class (according to Registrar-Gen.)					Probability (P) that the Observed Departures from Standard Incidence could have Arisen by Chance
	I	II	III	IV	V	
Flat-foot (A cases)	70		104	110	94	0·02>P>0·01
,, (B ,,)	79		96	107	139	0·01>P>0·001
,, (total)	73		101	109	111	0·01>P>0·001
Pes cavus	D		101	98	119	0·70>P>0·50
Hammer-toe	82		99	115	106	0·10>P>0·05
Hallux valgus	68		98	108	132	0·01>P>0·001
,, rigidus	149		91	103		0·20>P>0·10
Overlapping toes	68		98	122	118	0·05>P>0·02
Callosities	74		96	110	139	0·05>P>0·02
One or more of the above	60	80	100	108	112	0·001>P

The age-standardized ratios for all foot defects except hallux rigidus showed a marked social class gradient, with the highest incidence among unskilled and semi-skilled workers. But a separate analysis of the two varieties of flat-foot showed that it was only the B cases which tended to concentrate in the lower-income groups. A possible explanation of this difference is that economic factors are more potent to aggravate pre-existing conditions than to initiate new lesions.

The relatively level social class and age distributions of hallux rigidus are in marked contrast with the corresponding gradients for hallux valgus and rigid flat-foot. The contrast between hallux rigidus and hallux valgus corresponds to known differences between the aetiology of these two conditions, but that between hallux rigidus and rigid flat-foot is at first sight difficult to reconcile with the orthodox view that a flat-footed gait predisposes to osteoarthritis of the first metatarso-phalangeal joint. Provided, however, a *majority* of cases of hallux rigidus are due to causes other than flat-foot, there is no contradiction between the findings of the present investigation and accepted clinical opinion.

Table VI summarizes the results of an attempt to relate the risk of foot defects to strictly occupational influences, as distinct from risks associated with low economic status. Table VI abounds with examples of significant departures from standard incidence, but it is clear that many of these only reflect the earlier analysis by social class. There are, however, a few findings which cannot be accounted for on this score and suggest the possibility of more specific occupational influences. For instance, (1) shoe operatives had an exceptionally low incidence of hammer-toe but a high incidence of overlapping toes; (2) the group of lathe operators and testers had a high incidence of flat-foot and an unusually low incidence of hammer-toe; (3) transport workers had a high incidence of foot defects in general, and of flat-foot in particular; and (4) workers in farming and building had a large excess of pes cavus. With the data available it was not possible to explore these relationships further, but they offer promise that survey of footwear and "foot work" in selected industries would yield some interesting results.

Discussion

In the case of a disease, such as tuberculosis, which has been intensively studied from the statistical angle, even the minutiae of survey findings can usually be seen in their proper perspective. When, however, an epidemiologist attempts to use survey data for a study of foot defects he soon discovers that there is no ready-made context for his findings. The present study has resulted in a collection of miscellaneous facts which, like the pieces of a jigsaw puzzle, are tantalizingly rich in detail but lacking in general coherence. Nevertheless a start must be made some time, and, though the present investigation has left nothing fully proved, it does suggest some new lines of inquiry.

It is possible, for instance, that the variations in incidence of foot defects which have been found to be associated with variations in body build and social class reflect the fact that there is not, in this country, a wide enough range of shoe shapes and sizes to cope with the general need. Or that, if there is, the need remains unsatisfied because the public does not realize the dangers of ill-fitting shoes. This theory rests on two basic assumptions. The first is that the relationship between foot shape and body shape is such that persons of stocky build have feet which are disproportionately broad, and persons of slender build have feet which are disproportionately narrow. If this is so, then the fact that stocky men have emerged as bad risks in respect of flat-foot, and slender men as bad risks in respect of pes cavus and metatarsal deformities, may be due to the former being forced to wear shoes which are too long for the necessary width and the latter shoes which are too short.

The second assumption, which is introduced to explain the contrasts between tall and short men, is that the feet of tall men grow faster (as well as longer) than the feet of short men. The argument runs as follows: parents of children whose feet grow exceptionally slowly or exceptionally fast tend to misjudge the time taken to outgrow a new pair of shoes. As a result the slow growers (who are destined to be short men) spend most of their youth in shoes which are too big, and the fast growers in shoes which are too small. Finally, the social class gradient is accounted for by supposing that cheap shoes do more harm than expensive shoes, and that working-class parents find it particularly difficult to keep pace with the needs of growing children.

This is a highly speculative theory, and it is doubtful whether it would ever be possible to test it at all points, even if it proved acceptable to orthopaedic specialists. It will, however, have served its purpose if it shows how valuable it would be to know more about the relationship of body build to foot shape and the relationship of shoe habits to foot defects.

Summary

In a sample of 22,843 men aged 17 to 44 who were examined at Leicester in 1941, it was found that:

1. There was an increase with age in the incidence of rigid flat-foot, hammer-toe, hallux valgus, callosities, overlapping toes, and pes cavus. Hallux rigidus and mobile flat-foot showed a relatively even age incidence.

2. There was a real tendency for foot defects to occur in association with one another and with certain other skeletal defects.

3. Tall men suffered more often than short men from metatarsal defects (hallux rigidus excepted), but flat-foot more commonly affected short than tall men.

4. The risk of metatarsal defects increased continuously with increasing "linearity" of body build (as measured by the index $Ht \div \sqrt[3]{Wt}$). Flat-foot, on the other hand, was more common among men of stocky build.

TABLE VI.—*Relation Between Occupation and Incidence of Foot Defects. Standardized for Age (Standard Incidence = 100)*

Occupational Group	Main Social Class Represented	One or More Defect of Any Kind	Longitudinal Arch				Forefoot				Callosities
			Flat-foot			Pes Cavus	Hallux valgus	Hallux Rigidus	Hammer-toe	Overlapping Toes	
			All	A	B						
Professional and administrative	I and II	74§	68‡	62†	77	E	76	} 115	83	D	D
Commerce and finance	I ,, II	93	94	84	109	D†	78*		103	92	63†
Clerks and typists	I ,, II	79‡	65§	67†	D†	D	92		111	D*	D
Textile operatives	III	103	104	107	99	93	96	} 99	102	99	98
Boot and shoe operatives	III	102	109	110	107	112	95		79‡	125†	111
Engineers	III	100	97	113	60†	D	111		115	88	D
Lathe operators, testers, etc. (undefined)	III	95	123†	129†	111	D	96		58‡	D	D
Warehousemen, packers	III	109	97	96	99	D	131*		130†	D	134
Transport workers	III	116†	123†	120	130	E	93	} 92	119	128	128
"Other occupations"	IV	102	98	94	105	93	112		104	105	108
Farming, building, etc.	V	111	115	124*	100	155†	98		97	111	110
Unskilled	V	110	96	78*	128*	151†	132†		111	127	153‡
Probability (P) that observed departures from standard incidence could have arisen by chance		P<0·001	P<0·001	0·01> P>0·001	0·10> P>0·05	0·10> P>0·05	0·20> P>0·10	0·70> P>0·50	0·01> P>0·001	0·20> P>0·10	0·02> P>0·01

Where the contribution to the sum of χ^2 for all occupations made by any individual occupation would have been significantly large in a test based on one degree of freedom this is indicated by means of: * P<0·10; † P<0·05; ‡ P<0·01; § P<0·001.

5. Men in the lower social classes suffered more often than others from foot defects. The erroneous impression (which pre-dates the National Health Service) that all social classes are equally affected may have been due to a tendency on the part of well-to-do persons to seek medical advice for minor ailments more often than members of the working classes.

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INCIDENCE, ORIGIN, AND PREVENTION OF CERTAIN FOOT DEFECTS*

BY

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As the public know well, and hospitals' and chiropodists' reports confirm, many otherwise healthy adults suffer from foot trouble. A preliminary investigation in schools in Ealing (Craigmile, 1950) showed that many of the causes of adult foot disability were already present in the older schoolchildren. As a result of this, a routine foot inspection was begun in all maintained schools in the area. Until recently (Dykes *et al.*, 1952) there was no published report of the foot health of a normal population, and a survey of a factory in the area was made to determine the extent and chief causes of foot trouble in a normal working population. The results of this survey are in many respects confirmatory of the report of this survey at Luton, although undertaken on a different population and by different methods.

It soon became apparent that many foot troubles, while not present in the infant, began early in life and were due to stresses and strains imposed on an otherwise normal foot by modern conditions. Many of these lesions should be prevented, and an experiment, called the Ealing Contributory Shoe Scheme, was started in order to see how far good feet could be kept from developing defects and whether early defects already present would correct if the foot were given the best conditions for free growth.

This paper reports on these three surveys, which were made in an attempt to assess the most important foot defects in adults, their mode and time of origin in the child, and a suggested scheme to minimize their development.

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Survey I: Factory Workers

The factory employed men and women of all ages and in a wide variety of work. In the volunteer survey 358 employees were examined by two observers. Questions were asked about past and present foot trouble and an examination of the feet and shoes was made. The position of the employee at work was included in the record.

Table I shows the classified results. Rather surprisingly, the proportion of those with present foot discomfort was almost equal in the two sexes (29.6% of women and 27% of men). Both sexes showed an increase of complaints with age, and those who sat at their work had less trouble than the others. Women aged 40–49 had much more foot trouble than men of this age, and this was not related to obesity. The chief causes of pain in men were metatarsalgia (10%) and an ache in the long arch associated with a pronated forefoot (6.9%). In women the principal causes were bunions and hallux valgus (11.6%), metatarsalgia (5.8%), and a generalized ache in the long arch (3.1%). Corns caused pain in only 2.2% of both men and women, but this factory had a well-attended chiropody clinic.

Chief Causes of Pain

Metatarsalgia.—This was associated with increased callous formation and clawed toes. It was twice as common in men and was not related to position at work. Increasing the height of the heel can be shown to increase the thrust on the metatarsal heads. A 1-in. (2.5-cm.) heel gives an increased thrust of 18% of the body weight, and a 2-in. (5-cm.) heel gives a 41.5% increase. If, then, metatarsalgia were related to heel-height, it would be expected to occur more often in the women (average heel-height 1½ in.—3.8 cm.) than among the men (average heel-height ¾ in.—1.9 cm.), but the contrary was found.

Ache in the Long Arch.—This was related to forefoot pronation and is more common in the older age groups, in whom an increasing descent of the head of the talus has been shown (Hardy and Clapham, 1952).

Hallux Valgus and Bunions.—Hallux valgus occurred much more frequently in women, and the angle of deviation of the great toe, which appeared to be related to bunion formation, was in the region of 30 degrees. This external measurement corresponds closely to the radiographic measurements of the "critical angle of bunion formation" made by Hardy and Clapham, who found a

TABLE I.—*Distribution and Type of Foot Defects among Factory Workers*

Age Group (years)	Position at Work. No. of Persons										Type of Defect Found (Percentage)															
	Standers		Sitters		Walkers		Mixed		Total		Past Trouble		Present Pain		Hallux Valgus		Bunions		Crooked Toes		Valgus Ankles		Callouses		Corns	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
15– ..	2	17	—	19	—	3	4	8	6	47	50	12·2	15	15·7	—	—	—	—	33·3	27	16·7	44	16·7	44	16	36·4
20– ..	9	28	—	16	—	5	20	13	29	62	37·7	23·1	11	18·1	22	40	4	7·5	23	49	45	33·2	10	33·2	17·5	30
30– ..	5	11	—	6	4	1	14	5	23	23	33·2	21·7	21·7	21·7	21·7	21·7	5	21·7	32	50·8	43	50·8	56	50·8	15	56·6
40– ..	3	23	2	15	5	4	26	25	36	67	20	49·4	24	38	12	24	5	39·4	43	50·7	31	50	51	60	20	53
50– ..	8	7	1	3	8	4	8	11	25	25	44	32	32	43·4	24	32	12	43·4	43·4	48	36	41	48	60	43·4	30
60+ ..	3	1	1	1	1	—	7	1	12	3	48	66·6	48	33·3	40	33·3	8	—	68	100	80	100	68	—	50	33·3
Total ..	30	87	4	60	18	17	79	63	131	227	39·1	28·3	27	29·6	22·2	30	12·2	20	40·5	55	40	44	41·5	41	26	·2 39·4

mean angle of 28 degrees at the metatarso-phalangeal joint. Table II shows the preponderance of cases of bunions in which this angle is 30 degrees or more.

Table II.—*Relationship of Bunions to the Angle of Deviation at the Metatarso-phalangeal Joint. The Figures are for Women Only*

Age Group	No. of Cases of Hallux Valgus			
	Angle of 10–29 Degrees		Angle of 30–50 Degrees	
	No Bunion	Bunion Present	No Bunion	Bunion Present
15–39 years ..	50	4 (8%)	19	13 (68·4%)
40–65 „ ..	46	13 (28·2%)	47	32 (68·0%)

Survey II: Schoolchildren

The area under review covers both closely populated and semirural districts. About half the total school population was examined and all types of school were represented. The same two observers saw the children, and particular attention was paid to conditions likely to be precursors of adult foot trouble. Advice and treatment were given, where necessary at special sessions, and proved a valuable method of health education.

The results of the inspection of the 12,765 children are summarized in Table III.

Table III.—*Percentage of Certain Defects Found in Schoolchildren on Routine Foot Inspection*

Age Group	No. of Children	Proximal Hallux Valgus	Varus 1st Metatarsal	Cramped Toes	Valgus Ankles	Pes Cavus	Verrucae	Tinea	Unsatisfactory Footwear	Treatment Required	
										Chiropody	Minor Ailment Clinic
Infants, 5–7 years	Boys, 1,379	4·3	12·2	12·0	7·4	0·2	0·3	0	17·1	0·4	3·0
	Girls, 1,364	4·7	12·95	13·7	4·5	0	0·3	0			
Juniors, 8–11 years	Boys, 2,654	6·1	10·7	11·9	6·4	0·13	0·8	0·2	22·7	1·0	4·0
	Girls, 2,700	11·7	12·6	18 2	4·8	0	0·75	0·2			
Seniors, 12–15 or 16 years	Boys, 2,898	4·0	8·7	14·5	3·9	0·44	1·7	0·3	21·5	1·7	3·0
	Girls, 1,770	22·4	8·0	24·1	5·15	0·02	3·2	0·2	35·0	4·0	7.0

Hallux Valgus

This deformity is of two distinct types. The distal or interphalangeal type does not give rise to pain in adult life, and, while it appears to be congenital in some children, occurs with generalized cramping in association with short footwear (see Table IV). The proximal type is an important cause of pain in adult life, occurring most often in women. In schoolchildren this end-result can be seen in process of development (see Table V). A comparison of junior and senior children shows that three times as many girls had hallux valgus and with a greater mean angle of deflection. This implies that factors which result in many women suffering from bunions start to operate in the middle years of childhood and become fully active before the union of the metatarsal epiphyses.

In an attempt to assess the causes of this deformity various possibilities were considered: the intrinsic action of a short or a varus first metatarsal bone, or a pronated forefoot, and the action of extrinsic factors.

A short first metatarsal bone occurred in 39.4% of children and showed no age or sex differentiation; its presence was not closely related to hallux valgus. The intermetatarsal angle decreases with age (Keith, 1931) but a wider angle appears more common in females (Hardy and Clapham, 1952). Children with this variation from normal have difficulty in finding shoes broad enough for their feet, and, in order to eliminate this extrinsic factor, the combination of metatarsus primus varus and hallux valgus in children who wore good shoes was examined. These figures (Table VI) show no significant correlation. In other words, this suggests that metatarsus primus varus is not in itself an exciting cause of hallux valgus. It may, however, be a predisposing cause.

Table IV.—*Percentage of Cases of Proximal and Distal Hallux Valgus in Boys and Girls in Relation to Age and Suitability of Shoes Worn*

Age Group	Good Shoes			Bad Shoes		
	No. of Children	Proximal Hallux Valgus %	Distal Hallux Valgus %	No. of Children	Proximal Hallux Valgus %	Distal Hallux Valgus %
Boys						
Infants, 5–7 years	378	0·25	4·64	69	0·4	16
Juniors, 8–11 „	619	0·17	4·04	171	0·72	14·7
Seniors, 12–15 „	978	1·9	5·72	268	4·4	12·2
Girls						
Infants, 5–7 „	346	0·29	5·49	81	1·25	25·0
Juniors, 8–11 „	661	1·21	8·47	205	2·5	27·5
Seniors, 12–15 „	891	2·70	5·95	381	14·2	47·9

Table V.—*Percentage of Cases of Proximal Hallux Valgus Found, and the Angle of Deflection, at Different Ages*

Age Group	% of Proximal Hallux Valgus	Mean Deviation of Hallux	Range of Deviation
Infants, 5–7 years ..	0·1	5·0 degrees	3–18 degrees
Juniors, 8–11 „ ..	2·0	8·5 „	5–16 „
Senior boys, 12–15 years	2·4	10·7 „	5–28 „
Senior girls, 12–15 „ ..	8·7	16·5 „	7–35 „

The pronated forefoot appears to be related to hallux valgus of both proximal and distal types. In children who wore good shoes the probability of association was 0.01, and therefore unlikely to have arisen by chance.

There is an increase in the number of children wearing badly fitting shoes with age, the senior girls being far the worst group. A study of Table IV shows that there is a great increase in both types of hallux valgus with bad footwear. This increases with age, and is maximal among senior girls. Examination of the shoes showed two patterns which appeared particularly detrimental: the first type had sharply pointed toes, and the second was the "flattie" or "casual," which gives no support to the instep and therefore increases any tendency to pronation as well as cramping the toes.

Table VI.—*Relationship Between Metatarsus Primus Varus and Hallux Valgus in Children Wearing Good Shoes*

Sex	No. Examined	No. of Cases Metatarsus Primus Varus Alone	No. of Cases Hallux Valgus Alone	No. of Cases Combined Defect	χ^2	Probability
Boys	1,875	445	85	34	0·611	0·80 (Not significant)
Girls	1,962	411	122	49	0·518	0·90 (Not significant)

Deformed Toes and Flat Foot

Hammer-toes and mallet-toes showed a constant percentage of 1.7 for all ages. While about 99% of the children over 10 years of age have some twisting of the fifth toe, this was symptomless in many cases. Cramping of all toes associated with signs of pressure was found in about 10% of the children and was closely associated with tight shoes.

Of the main types of flat-foot, the stable low-arched foot was very common and, as in the adult, it was symptomless. Pronation of the forefoot is, however, important as a potential cause of future pain. It is very common in the pre-school group, but only about 5% of cases persist into school life. Pronated forefeet are also closely associated with hallux valgus.

Pes Cavus

Pes cavus may be congenital or acquired, and of the latter type, as well as those secondary to neuromuscular causes, there are many idiopathic cases. These latter are of interest in that they, alone of all structural foot defects, are more common in boys than in girls. This pes cavus was not related to heel-height, but was associated with short shoes. (B.B.S.A.T.R.A. Research Report No. 107).

Survey III : Ealing Contributory Shoe Scheme

This scheme was open to all children attending one welfare centre and one school in the area. It was designed to be financially self-supporting. For a lump sum, payable in instalments before entry, the child was able to obtain three pairs of walking-shoes and one pair of sandals each year. Careful medical supervision of the feet was undertaken at intervals of ten weeks throughout the year, and a general physical examination was made on entry to the scheme.

The scheme was made possible by the co-operation and interest of Messrs. James Southall & Co., who supplied the shoes, and of their two agents in the area.

At the first examination it was decided whether the standard shoes should be worn or if any modifications were required; this was noted on the voucher with which the shoes were purchased. In special cases joint consultations were made with the shop managers or the technical adviser to Messrs. Southall. Assistants who had special training in children's fittings supplied the shoes from a full range of four fittings to each half-size.

The scheme ran for two years, fresh entrants being accepted for the second year, and 164 children were studied (Table VII). The information obtained may be divided into non-medical data and facts of more direct medical value. As had been estimated, three pairs of strong shoes were just enough for the needs of most children. The amount of repairs varied widely, and rubber composition appeared to be the most hard-wearing material. A record of the fittings required showed that at least three fittings to each half-size were necessary to obtain an accurate fit.

TABLE VII.—*Number of Children who Joined the Shoe Scheme, the Cost of the Scheme, and the Annual Expenditure on Shoes of a Sample of Children in the Borough, in the Previous Year*

Age in Years	No. of Children	Annual Cost of Scheme	Yearly Expenditure of "Average" Child
2–	88	£2 17s. 0d.	£2 18s. 0d.
5–	36	£4 17s. 0d.	£4 3s. 0d.
8–	32	£5 9s. 6d.	£5 11s. 0d.
11–15	8	£6 10s. 0d.	£6 14s. 0d.
Average ..	164	£4 18s. 4½d.	£4 16s. 6d.

TABLE VIII.—*Number and Kind of Defects Found in the Feet of Shoe-scheme Children*

Defect	No. of Cases		
	At Start	After 6 Months	After 1 Year
Hallux valgus	31	26	12
Cramped toes	46	20	8
Metatarsus varus ..	30	23	13
Pronated forefoot ..	29	17	16
Corns and callouses ..	30	8	3
Out-toeing	18	5	3
In-toeing	8	2	—
Knock-knees	21	7	3
Verrucae	6	—	—
Other (blisters, chilblains, etc.)	31	9	11
Total	250	117	69

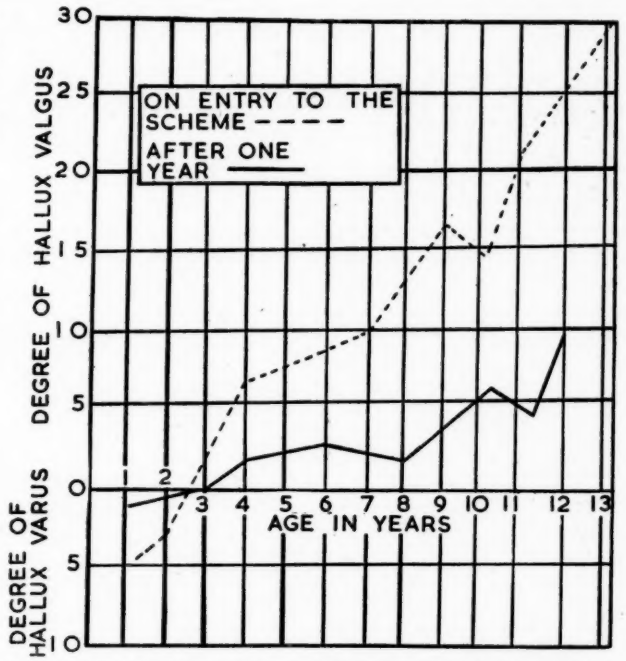

FIG. 1.—Graph showing the average angulation of the great toe at the metatarso-phalangeal joint at various ages.

Pedograph Records.—A pedograph was made on entry to the scheme and after one year; it proved a useful measure for demonstrating decreasing pronation of the forefoot and the redistribution of weight in the foot.

Defects and Deformities

Table VIII shows the decrease in number of defects during one year and illustrates the rapid decline in foot troubles when expert advice is available. Certain conditions showed a spontaneous recovery without treatment other than well-fitting shoes and socks. The younger the

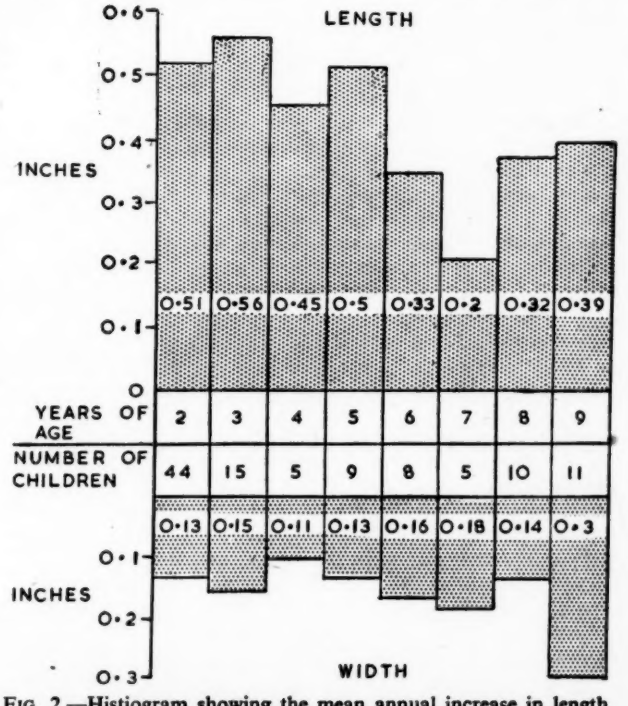

FIG. 2.—Histiogram showing the mean annual increase in length and width of the foot for each year of age.

child the quicker was the return to normal. These defects were corns, callosities, cramped toes, and proximal hallux valgus. The angle of the hallux was studied, and 48 children showed a deviation of more than 2 degrees in either direction. There was a marked decrease in the angles of deviation after one year (see Fig. 1).

Growth Rates

Measurements were made of the rate and periodicity of growth, and the results in 107 children who attended regularly for at least one year are shown in Fig. 2. The rate

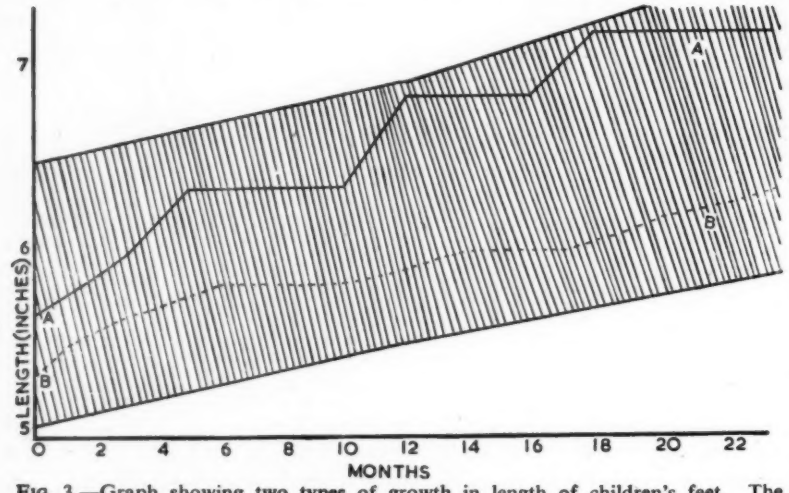

FIG. 3.—Graph showing two types of growth in length of children's feet. The shaded background shows the range of measurements found in the shoe-scheme children of the same age.

in girls and boys was fairly close, the average increase in length being just under ½ in. (1.3 cm.) a year; this corresponds to one whole size in shoes. The periodicity of growth is interesting, and Fig. 3 shows the types which occur. The commonest type was a curve showing alternating periods of growth and quiescence. This may be an annual or a biannual spurt. Child A shows both types over the two years; a regular slow growth, illustrated by Child B, was less common. The period of the year at which most growth occurred was the summer (June–August), while the autumn (September–November) was the usual quiescent period.

Discussion of the Three Surveys

Many adults suffer from pain in their feet. This is borne out by the demand for chiropody treatment in private practice and by the first survey on adult factory workers. Such discomfort must have an appreciable effect on the general health, temper, and work of the sufferer, while the final result on the country's economics is an interesting imponderable. This survey also suggests that the principal causes of pain are hallux valgus and bunions, pain in the long and transverse arches, and corns. The first-named occurs chiefly in women.

The results of the school survey show that these defects begin to develop during the years of childhood and increase progressively with age. While no single cause for the predominance of hallux valgus in girls is apparent, the figures shown suggest that both valgus ankles and bad footwear, which are more common in girls than in boys, play a part in producing this deformity, but the preponderance of valgus ankles is not in itself sufficient to account for the greater number of cases of hallux valgus in girls. That idiopathic clawed foot is more common in boys than in girls is probably related to the predominance of metatarsalgia in men. One theory of development may be suggested: that the rounder shape of a boy's shoe, when short, exerts equal pressure on all toes, causing retraction and dorsiflexion, while a girl's more pointed shoe presses mainly on the fifth and first toes.

The experimental contributory shoe scheme has shown that it is both possible and practicable to run such a scheme for supervising the care of children's feet and, by so doing, to diminish the amount of foot trouble in children. While its inherent principles are sound, the scheme has certain disadvantages. First, that while prices are unstable it may be impossible for manufacturers to budget accurately for a year ahead; secondly, it is a pity to limit the scheme to one firm only; and, thirdly, comparatively few parents have taken advantage of it, as many felt that the prices were beyond their reach. This assumption was not entirely reasonable, for the prices in the scheme compared very closely with the average amount spent on footwear in the preceding year in the same district (Mayers, 1950). Nevertheless a modification of this scheme suggests a line of approach to the problem of the great number of painful and defective feet in the adult population.

Conclusions

A survey to study the main causes of foot trouble in the adult suggests that bunions and hallux valgus, metatarsalgia, long-arch pain, and corns are the chief types of foot disability in healthy adults. An examination of schoolchildren has shown that these defects begin in the later years of childhood. An attempt to maintain foot health by providing children with good footwear and by supervising their feet during the growing period showed that it is possible to prevent deformities and that certain early defects will correct spontaneously, given freedom for normal growth.

It is my pleasure to thank the Health Department of Middlesex County Council for facilities to carry out this research; in particular, Dr. W. G. Booth, area medical officer, Area 7, Middlesex County Council, to whom the Ealing Contributory Shoe Scheme owes its origin; also the British Boot, Shoe, and Allied Trades Research Association for loan of instruments; the Managing Director and Technical Adviser of "start-rite" shoes; to Mrs. Murton, S.R.N., for help in examination of the subjects.

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"It is regrettable that the position in relation to the institutional care of mental defectives has steadily worsened over the past four years. There is now a waiting-list of more than 420 patients for admission to institutions, as compared with 170 in 1948. The county council provides domiciliary supervision for all mental defectives in the county, and there are eight occupation centres where defectives may go daily for training and occupation, but this is no adequate substitute for institutional accommodation in many cases. There are numerous households where the defective child or adolescent is an intolerable burden and where only segregation in an institution will meet the case. The need for additional institutional beds for such patients is most urgent and should have a high priority in planning the use of available resources in manpower and money."—From the Report for 1952 of the Essex County Medical Officer of Health, Dr. H. K. Cowan.

THE 17-HYDROXYCORTICOSTERONE CONTENT OF HUMAN ASCITIC FLUID

BY

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In spite of many investigations uncertainty still exists about the quantity of adrenal cortical hormone present in human blood and other human body fluids. Most work in this field has been done on animals, and particular attention has been paid to the blood leaving the adrenal gland by the adrenal vein, since the highest concentrations of adrenal hormones may be expected in such blood. Both chemical and biological methods of assay have been applied, but neither has been entirely satisfactory, since chemical methods have not in general been sufficiently specific, and the biological methods have not been sensitive enough to respond to the very small quantities of active hormone present in circulating blood.

The Literature

One of the earliest estimates was that of Hemphill and Reiss (1947), who used a chemical extraction of blood and subsequent estimation of the reducing power of the steroid fraction. They worked mainly on rats, but found 0.21 to 0.43 mg. per 100 ml. in human blood. This early estimate must now be regarded as much too high.

Paschkis, Cantarow, and Boyle (1949) reported the detection of small amounts of adrenal hormone in arterial plasma of the dog. They used the method of glycogen deposition in the liver of the adrenalectomized mouse which had been developed by Venning, Kazmin, and Bell (1946). In the following year Paschkis, Cantarow, Walkling, and Boyle (1950) reported finding values of 14 to 50 μg. per ml. of dog adrenal-vein blood, the activity being expressed in terms of 11-hydrocorticosterone (compound A) acetate. They could also demonstrate biological activity in the peripheral blood of the dog.

In 1950 also, Nelson, Reich, and Samuels succeeded in isolating and identifying compound F of Kendall (17-hydroxycorticosterone; hydrocortisone) in the blood of the adrenal vein. Brownell, Hartman, and Liu (1951), who used the Venning glycogen deposition method, reported finding biological activity in dog adrenal-vein blood, but they were unable to detect any activity in the peripheral blood. Thus the earlier work of Paschkis and his colleagues on peripheral blood was not confirmed.

The relatively higher concentrations of hormone in adrenal-vein blood enabled more rapid progress to be made than was possible with peripheral blood, and Pincus, Hechter, and Zaffaroni (1951) were able to extract adrenal steroids from dog adrenal-vein blood in amount sufficient to allow of analysis by paper chromatography. In the dog the steroids identified were mainly 17-hydroxycorticosterone and corticosterone. The concentration of these after adrenal stimulation by A.C.T.H. rose as high as 55 μg. of each per 100 ml. Cortisone was present in a concentration less than 10 μg. per 100 ml., and was regarded as a metabolite, 17-hydroxycorticosterone and corticosterone being the main products.

Following up their identification of 17-hydroxycorticosterone in dog adrenal-vein blood, Nelson, Samuels, and Reich (1951) developed a chemical method based on the purification of the extracted adrenal steroids on a chromatographic column and subsequent measurement of the eluted adrenal steroids by means of a colour reaction with phenylhydrazine and sulphuric acid. This colour reaction had been developed by Porter and Silber (1950) and had been shown by them to be specific for steroids having a 17-21-dihydroxy, 20-keto grouping. Both cortisone and 17-hydroxycorticosterone give the typical reaction, but it is given only weakly by corticosterone. Compounds giving this reaction are often called 17-hydroxycorticosteroids. The reaction cannot be regarded as entirely specific for active hormones, since some other products of adrenal steroid metabolism, notably tetrahydrocortisone, also give a strong reaction with the reagent but are biologically inert. Using the reaction on a micro-scale, Nelson and Samuels (1952), and Nelson, Willardson, Tyler, and Samuels (1951) found 4 to 6 μg. of 17-hydroxycorticosteroid per 100 ml. of human venous blood and 9 to 11 μg. in human arterial blood. Both figures rose after A.C.T.H. While some of this was probably 17-hydroxycorticosterone an unknown proportion may have been tetrahydrocortisone. This latter metabolite presumably occurs in blood, since it is present in large amount in urine, and has been identified in a peritoneal dialysate by Savard, Kolff, and Corcoran (1952).

Complication rather than simplification has ensued more recently. Thus Bush (1953) showed that the adrenal steroids differed in nature in different species of animal, some having much 17-hydroxycorticosterone and little corticosterone, and other species more of the latter than the former. Sweat and Farrell (1952), using a microchromatographic technique and subsequent detection of the steroids by fluorescence, developed a method sensitive to 0.25 μg. They found 4 to 8 μg. of adrenal steroid in the adrenal-vein plasma of stressed rats, but were unable to find any in peripheral blood of adrenalectomized rats. In the adrenal-vein plasma of dogs under stress they found 3 μg. of a steroid resembling 17-hydroxycorticosterone and 1 μg. of a corticosterone-like steroid.

At the same time Pincus, Romanoff, and Romanoff (1953) were producing data indicating the complexity of the problems involved in this and allied aspects of adrenal metabolism, for they were able to detect 35 different neutral lipoids in hydrolysed human urine, and similar compounds were found in human peripheral blood. Among the most important of these were corticosterone (compound B), 17-hydroxycorticosterone, cortisone, pregnane 3-11-17-21 tetrol 20-one, and pregnane 3-17-21 triol 11-20 dione (tetrahydrocortisone).

Zaffaroni and Burton (1953) have analysed a large volume of dog adrenal-vein blood from an animal stimulated by A.C.T.H. They found 130 μg. of 17-dehydroxycorticosterone and 95 μg. of corticosterone per 100 ml. of blood. Only traces of other compounds were found, but the method they used would not have detected some of the important inert metabolites such as tetrahydrocortisone.

The present position may therefore be summarized as follows.

Both corticosterone and 17-hydroxycorticosterone are present in appreciable quantity in adrenal-vein blood of experimental animals. Cortisone is not usually found. The most refined chemical methods indicate the normal presence of 4 to 6 μg. of 17-hydroxycorticosteroid in 100 ml. of peripheral venous blood and 9 to 11 μg. per 100 ml. of arterial blood. A considerable part of this seems to be 17-hydroxycorticosterone, but an uncertain fraction is metabolites which give the same colour reaction but are biologically inert—for example, tetrahydrocortisone. Biological assay indicates the presence of some active adrenal steroid in dog adrenal-vein blood, but no certain activity has been established in peripheral blood in either animals or man.

It seemed to us that useful light might be thrown on the problem by analysis of human ascitic fluid. Although ascitic fluid is not a normal body product it can be obtained in relatively large quantities, sufficient to make a biological assay feasible if the content in active hormones is 1.5 μg. or more per 100 ml. We have found activity in excess of this figure in five out of ten ascitic fluid samples tested.

Methods

Samples of ascitic fluid have been obtained from suitable patients in volumes of 3 to 7 litres. These samples were extracted and the steroids concentrated into a volume small enough for injection into mice by a method employed by Bush (1952) for blood. The ascitic fluid was extracted by shaking four times with separate lots of chloroform, each representing 15% of the volume of the sample. The four extracts were combined and evaporated under reduced pressure at a temperature below 50° C. to small volume. To the residue of 5 to 10 ml. was added 200 to 400 ml. of acetone and a few drops of saturated magnesium chloride. The mixture was cooled overnight in the refrigerator. After filtration the acetone solution was distilled down to a small volume (3 to 5 ml.). This residue was taken up into 100 ml. of 70% aqueous ethanol and washed three times with 10-ml. portions of light petroleum to remove excess fats. The ethanol solution was evaporated under reduced pressure to dryness, dissolved in a small volume of chloroform, and transferred to a small tube in which it was evaporated to dryness by a stream of nitrogen to await injection.

For bio-assay the method described by Cope, Boysen, and McCrae (1951) has been used. This method makes use of the fact that cortisone-like hormones lower the number of eosinophil cells in the blood of adrenalectomized mice. An extract equivalent to 1,500 ml. of ascitic fluid was injected subcutaneously into each adrenalectomized mouse. For injection the extract was dissolved in propylene glycol, using 0.1 ml. for each 1,500 ml. of ascitic fluid represented. Four volumes of saline were then added, so that the final volume was such that each mouse received a 0.5-ml. injection of this 20% propylene glycol solution.

The eosinophil cell drop in the injected adrenalectomized mice was measured at four and six hours, the greater drop being taken as the significant one. The equivalent activity of cortisone was read off from a calibration curve prepared by injecting cortisone acetate in similar and constant volume of 20% propylene glycol, but in varying dosage into adrenalectomized mice.

Results

The results obtained with these extracts are summarized in the accompanying Table. Ten samples of human ascitic fluid have been separately extracted and tested, most of these being of sufficient volume to provide material for three mice. Five of these extracts showed unequivocal evidence of eosinopenic activity. Two extracts, both from the same patient, showed no trace of biological activity, and in the remaining three the presence of activity was equivocal.

Patient	Disease	Vol. per Mouse (ml.)	No. of Mice	Toxicity	Mean Drop Eosinophils	Equivalent Cortisone Content (μg. per 100 ml.)
1 Fr	Cirrhosis	1,500	3	++	No drop	Nil
2 Fr	,,	1,500	3	+	,,	,,
3 Re	,,	1,700	2	0	"77%"	4·4
4 Pe	Carcinoma of peritoneum	1,600	3	++	62%	3·1
5 Pe	,,	1,500	2	+	11%	<1·5
6 Du	Tricuspid incompetence	1,560	2	0	68%	3·8
7 Du	,,	1,500	3	0	77%	5·0
8 Ha	Cirrhosis	1,560	3	0	74%	4·5
9 Du	Tricuspid incompetence	1,500	2	+	15%	<1·5
10 Du	,,	1,500	3	+	20%	<1·5

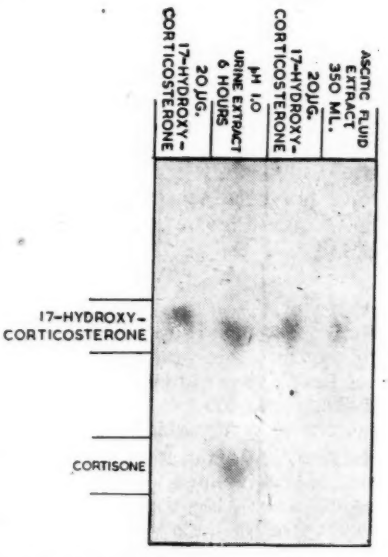
+ toxicity = Well-marked sedation without loss of consciousness. ++ toxicity = A light coma from which the animals recovered in a few hours.

Some of these extracts were rather toxic to the mice, producing lethargy and sometimes light narcosis. This effect was at first thought to be due to traces of the magnesium chloride used in the preparation of the extract being carried into the final residue, but efforts to remove this magnesium did not remove the toxicity. There was no relation between this toxicity and the magnitude of the eosinopenic response. Long-acting anaesthetics such as pentobarbitone sodium do not influence the eosinophil response to cortisone in the adrenalectomized mouse. The degree of toxicity of the extracts is indicated in the Table.

It will be noted that although both ascitic fluid samples obtained from patient Fr were completely devoid of activity, yet in patients Pe and Du eosinopenic activity varied in samples of ascitic fluid removed from the same patient at different times. No explanation can be offered for this apparent variation, since the method of making the extracts was the same in all.

Discussion

The data obtained indicate that, although the amount of biologically active adrenal hormone extractable from human ascitic fluid appears to be variable, it does not usually exceed 5 μg. per 100 ml. In half the extracts examined it was much less than this, being below the level necessary for reliable detection by the methods used. Our previous experience with this bio-assay technique indicates that the variations in activity observed are much greater than could be due to errors in the method of assay.



Comparison of paper chromatograms of both urine and ascitic fluid extracts.

Some information has been obtained on the nature of the hormone responsible for this biological activity. Extensive search by many investigators has failed to reveal any hormones other than cortisone and 17 - hydroxycorticosterone, which lower the eosinophil count in the blood of adrenalectomized mice. Portions of four of the ascitic fluid extracts used in the present study have been submitted to analysis by paper chromatography, using the solvent systems developed by Burton, Zaffaroni, and Keutmann (1951). Whereas a substance behaving like 17-hydroxycorticosterone could be demonstrated in all of the extracts examined, cortisone was usually absent completely. It was indeed detected only in faint trace in a single extract. Urine, in contrast, usually contains both 17-hydroxycorticosterone and cortisone. Actual paper chromatograms of both urine and ascitic fluid extracts are compared in the accompanying illustration. The 17-hydroxycorticosterone found in these extracts was identified by the following points: (1) Its rate of flow in the chromatogram was identical with that of an authentic sample of free 17-hydroxycorticosterone. (2) It reduced the blue tetrazolium reagent like the authentic compound. (3) It absorbed ultra-violet light at 240 mμ. (4) The compound behaving identically with this which is present in urine has been injected into mice and shown to have strong eosinopenic activity.

Sufficient of one extract (No. 10) was available to permit a chemical estimate of the quantity of 17-hydroxycorticosterone present by measurement of the amount of tetrazolium reagent reduced at the appropriate point on the chromatogram. The estimate of 1.8 μg. per 100 ml. agrees well with the traces of activity found in the biological test, for larger quantities in the extract would have given an unequivocal biological response.

As corticosterone itself has been identified in the blood of many mammals, it is possible that this compound also is present in human ascitic fluid. No search for this substance was made in the present work, because no sample of

authentic corticosterone was available for comparison. Corticosterone, however, is reported to have only a slight eosinopenic effect, which would not contribute appreciably to the biological activity detected in these ascitic fluid extracts.

It may be concluded, therefore, that almost all of the biological activity observed is due to the content of 17-hydroxycorticosterone, and that this varies in different samples of ascitic fluid from zero to about 5 μg. per 100 ml. Cortisone itself does not contribute to the biological activity in significant degree.

It is, of course, clear that one cannot assume that the hormone content of ascitic fluid is necessarily the same as that of circulating blood. Ascitic fluid may, however, be regarded as representing a form of extracellular fluid. Its hormone content may be indicative of the adrenal hormone content of extracellular fluid in general, a content which must be of more direct importance to living cells than is the hormone content of the blood. Our inability to demonstrate any hormonal activity in the two samples from patient Fr raises the possibility that conditions may sometimes exist in which adrenal cortical hormone diffuses with difficulty from the blood into the extracellular fluid. Such a state could account for the fact that rheumatoid arthritic tissues and joints respond promptly to cortisone or 17-hydroxycorticosterone therapy, although all the evidence suggests that adrenal cortical function is normal in this disease. While this suggestion is purely speculative at the present time, further investigation of the hormonal content of human ascitic fluid should prove of considerable interest, in so far as it is representative of an extracellular fluid.

Summary

The adrenal cortical hormone content of human ascitic fluid has been measured biologically, using the power of such hormones to lower the level of circulating eosinophil cells in adrenalectomized mice.

Of ten samples of ascitic fluid tested, five showed activity equivalent to between 3 and 5 μg. of cortisone per 100 ml. In two samples from one patient no activity at all could be detected. In the remaining three activity was equivocal and less than 1.5 μg. per 100 ml.

17-hydroxycorticosterone (compound F) was detected by chromatographic analysis in all four samples in which it was sought, but cortisone was found only as a faint trace in a single extract. The biological activity is apparently due almost entirely to the 17-hydroxycorticosterone, only a negligible part being due to cortisone.

Grateful acknowledgments are due to the Medical Research Council for a grant for Miss B. Hurlock; to Professor Schuman (Ciba) for a generous gift of 17-hydroxycorticosterone, and of free cortisone; and to Miss Mary Standring for much technical assistance.

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PIPERAZINE IN THE TREATMENT OF THREADWORMS IN CHILDREN

REPORT ON A CLINICAL TRIAL

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The successful use of piperazine in the treatment of threadworms was first recorded by Mouriquand, Roman, and Coisnard (1951) and later by Turpin, Cavier, and Savaton-Pillet (1952). Mouriquand *et al.* used piperazine hydrate in solution, while Turpin *et al.* chose piperazine diphenyl-acetate in the form of glutenized granules. In most instances oral dosage was supplemented by the use of piperazine suppositories. The clinical trials carried out by both groups of workers were preceded by successful preliminary experiments upon the mouse *Aspiculuris* or *Syphacea*. In the clinical trials Mouriquand *et al.* reported a high proportion of cures in 18 patients, while Turpin *et al.* recorded one definite failure out of 41 patients.

We ourselves decided to carry out clinical trials following successful experiments with piperazine hydrate against *Aspiculuris* in the mouse (Standen, 1953). As a comparative standard, gentian violet was also included, and, in addition, diphenan, which has achieved considerable popularity on account of its lack of toxic side-effects. Laboratory tests had failed to demonstrate oxyuricidal properties in diphenan. These results were in keeping with the clinical findings of Miller and Choquette (1950), Beaver and Young (1950), Dowsett and Brown (1953), Jung and Beaver (1953). In contrast, Killingsworth *et al.* (1952), using diphenan in conjunction with hexylresorcinol enemas, reported 77% cures, while Bumbalo *et al.* (1953) reported 30% cures with diphenan alone. Killingsworth *et al.* and Van Someren (1939) both quote Schulemann (1920) as stating that diphenan breaks down in the small intestine to form para-benzylphenol, and that this kills oxyurids in 5–10 minutes at 1:4,000 dilution. In fact, Schulemann was working with "Strudelwurmen," which are free-living turbellarians and not in any way related to oxyurids in particular nor to nematodes in general. It is considered that this mistranslation of Schulemann's work should be recorded, since it appears to be in danger of perpetuation in the literature.

Clinical Tests

The material used in the tests consisted chiefly of children admitted to hospital for medical or surgical reasons, and these were identified as cases of *Enterobius* infection by microscopical examination of adhesive "cellophane" swabs of the perianal area. Swabbing was carried out in the morning before the children were bathed or used the toilet, and was repeated for seven days unless a positive result was obtained earlier. In addition, previously established cases of oxyuriasis were included. For purposes of comparative drug effect the children were treated in four groups, each group receiving piperazine, gentian violet, diphenan, or a lactose placebo.

Treatment

(*a*) *Piperazine.*—Used in the form of piperazine hexahydrate embodied in a flavoured syrup. The children receiving piperazine were divided into two groups, one receiving 100 mg. and the other 250 mg. per day per year of life, the drug being given in divided doses, morning and evening. Treatment continued for seven days, and a second similar course was given after seven days' rest.

(*b*) *Gentian Violet.*—Given as sugar-coated pills at a dose level of approximately ¼ gr. (11 mg.) daily per year of life in divided dosage for seven days and repeated after seven days.

(*c*) *Diphenan.*—Given as whole or fractions of plain 500-mg. tablets. Owing to difficulty in subdivision of tablets to suit each year of age, the children were arranged in broad age groups. Inevitably this meant a range in dosage from approximately 100–300 mg. t.d.s. per year of life in the lower dosage group and approximately 200–600 mg. t.d.s. for those at higher dosage. The course of treatment was for seven days, and was repeated after seven days' rest.

(*d*) *Lactose Placebo.*—A control group was considered highly desirable in order to determine the degree of spontaneous cure. The placebo was given morning and evening in two courses of seven days as with the other drugs.

Follow-up

Swabbing of the perianal area with adhesive cellophane was begun 14 days after completion of the second treatment period, and was continued each morning for seven successive days. Any single swab showing one or more ova indicated failure to cure, while seven successive negative swabs formed the criterion for cure.

Hygienic Precautions

In most instances the children received treatment as outpatients, and it was considered unrealistic to expect parents to adhere uniformly to strict hygienic precautions. Consequently, beyond instruction concerning general cleanliness, no special precautions were imposed. Thus the trials were carried out under conditions that would normally prevail in an average household.

Toxicity and Side-effects

(*a*) *Piperazine.*—During the first quarter of the century piperazine was widely used in the treatment of gout and allied conditions, but it has fallen into disuse because of ineffectiveness in these complaints. Consequently many reports have been published concerning its use in this respect and no important toxic effects have been recorded. Absence of toxicity has been reported by numerous authors, notably Frankel (1921), Gadamer (1924), Fayard (1949), Mouriquand *et al.* (1951), and Cavier (1953). Recent pharmacology and toxicity studies in laboratory animals (De Beer, unpublished) failed to elicit any significant toxic effects. In our experience during clinical trials only one case showed intolerance. At a dose level of 58 mg./kg. per day, this child complained of loose stools. When treatment was discontinued the diarrhoea ceased immediately. The drug was, in fact, found to be extremely well tolerated even up to dose levels of 150 mg./kg. daily. This higher dose relates to treatments of ascariasis, which will form the subject of a further communication.

(*b*) *Gentian Violet.*—Out of 20 cases treated two complained of abdominal pain and one experienced nausea and vomiting during the first week of treatment. Otherwise no side-effects were reported.

(*c*) *Diphenan.*—Treatment with diphenan produced no toxic side-effects.

Table showing the Comparative Effectiveness of Drugs Used in Clinical Trials Against Enterobius vermicularis Infections in 136 *Children*

Drug	Daily Dose per Year of Life	Age Range	Total No. Treated	Cases Followed Up			
				Total No.	No. of Cures	No. of Failures	% Cures
Piperazine hydrate	100 mg.	1½–11 3 adults	44	35	19	16	54
	250 mg.	1½–13 2 adults	64	42	35	7	83
Gentian violet	1/6 gr. (11 mg.)	2½–12	38	20	14	6	70
Diphenan	100–300 mg.	1½–11	34	22	4	18	18
	200–600 mg.	11	7	1	—	1	—
	Combined results	1½–11	41	23	4	19	17
Lactose placebo	—	2–7	36	16	3	13	19

Results

Comparative Results.—At 100 mg. per day per year of life piperazine hydrate gave a lower cure rate than gentian violet at ¼ gr. (11 mg.) daily per year of life (see Table)—that is, 54% and 70% respectively. At the higher dose level of 250 mg. per day per year of life the cure rate for piperazine hydrate was much enhanced, giving 83% cures out of 42 cases treated. The efficiency of diphenan at both dose levels (see Table) closely resembled that of the lactose placebo—that is, 17% out of 23 cases and 19% out of 16 cases respectively.

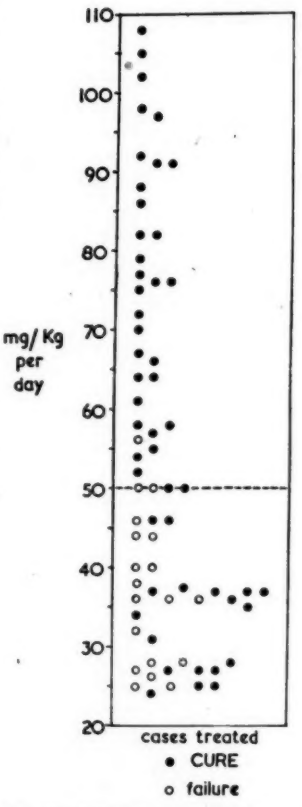

Chart showing relationship of dose of piperazine hydrate in mg./kg. per day to cure in 69 cases of oxyuriasis.

Analysis of Piperazine Results.—It was appreciated that considerable weight variation occurred within each age group tested, and analysis of the total results of piperazine hydrate tests at both dose levels (see Fig.) shows that on a weight/dose/cure ratio a cure rate of 97% was obtained where the daily dose exceeded 50 mg./kg. body weight.

Conclusions

The results obtained from the clinical trial of piperazine hydrate, gentian violet, diphenan, and a lactose placebo as control showed that while gentian violet had a marked oxyuricidal effect (70% cures) at a dose level of ¼ gr. (11 mg.) daily per year of life, this was well surpassed by piperazine hydrate syrup when the dose level was in excess of 50 mg./kg. per day, and the cure rate reached 97%. Though diphenan gave a cure rate of 17% at a dosage of 100–600 mg. daily per year of life, this apparent oxyuricidal effect was discounted by the fact that 19% cure was obtained with a lactose placebo control. The latter indicated that a spontaneous clearance of threadworms may be expected in approximately 19% of infections. Thus piperazine hydrate syrup proved to be the most effective, while producing negligible side-effects; gentian violet was less effective, and was also undesirable on account of its nauseating effects and staining properties; diphenan was ineffective. It is concluded that piperazine hydrate, at a dose level of 50–75 mg./kg. per day, is the drug of choice for the treatment of oxyuriasis in children.

Summary

In clinical trials of piperazine hydrate, gentian violet, and diphenan against oxyuriasis in 136 children, piperazine hydrate syrup and gentian violet showed marked oxyuricidal properties, while diphenan was inactive.

Owing to lack of toxicity and side-effects, to ease of administration, and to its excellent therapeutic properties, piperazine hydrate syrup at a dose level of 50–75 mg./kg. per day is considered to be the drug of choice for oxyuriasis in children. Of 31 children treated at levels greater than 50 mg./kg. daily 97% were cured.

The use of suppositories is unnecessary.

Spontaneous cure may be expected in 19% of cases of oxyuriasis.

The facilities provided by Dr. Philip R. Evans in the Department of Child Health at Guy's Hospital and the Evelina Hospital, London, are gratefully acknowledged. The guidance and advice of Dr. R. C. MacKeith, Guy's Hospital, are deeply appreciated. Without the co-operation of the medical and nursing staffs at these two hospitals this work could not have been completed, and to them our greatest thanks are extended.

The piperazine hydrate used in these trials was provided by Messrs. Burroughs Wellcome and Co. as "antepar" elixir.

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EXPERIMENTAL CHEMOTHERAPY OF OXYURIASIS

BY

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The two drugs most commonly used in the treatment of oxyuriasis are gentian violet and diphenan. From time to time claims of efficacy in clearing threadworms have been made for other substances, notably aluminium 8-hydroxyquinoline ("nyxolan"), N-*iso*amylcarbaminic acid-3-methyl-6-*iso*propyl phenyl ester ("egressin"), and garlic preparations. Owing to the length of the life cycle and the possibilities of auto-infection, properly controlled clinical trials against *Enterobius* (*Oxyuris*) *vermicularis* are extremely complicated. The eight weeks or so required for diagnosis, treatment, and follow-up is longer than children usually remain in hospital, and any trials started under the control and supervision of the medical and nursing staff must be continued with the co-operation of the parents. The difficulties inherent in such an arrangement probably account for the relatively few occasions upon which adequate clinical trials have been made with potential oxyuricides. Obviously some laboratory method of screening drugs of this kind is desirable, so that these cumbersome clinical trials may be initiated only when justified by experimental evidence.

As no laboratory animal has been found that will act as host to *E. vermicularis* the oxyurids of rodents have been employed for chemotherapeutic trials. The laboratory evaluation of egressin was carried out using *Passalurus ambiguus* in the rabbit (Eichholtz and Hotovy, 1950); *Aspiculuris tetraptera*, oxyurid of the mouse, was used for study of the oxyuricidal properties of antibiotics (Wells, 1951a, 1951b, 1952a, 1952b); *Syphacia obvelata* in the mouse was used by Chan (1952) for screening a number of potentially active substances, while Turpin *et al.* (1952) tested piperazine against both *Aspiculuris* and *Syphacia*. Mouriquand *et al.* (1951) used piperazine hydrate against *A. tetraptera* in the mouse.

A. tetraptera occurs naturally in the caecum and rectum in many laboratory strains of white mice. For the experimental work here described it was decided to use such natural infections with this parasite and to carry out a series of tests on substances of reputed activity against human threadworms. Tests on certain closely related substances were also to be included. By this means it was hoped to determine whether tests against *A. tetraptera* in the mouse would provide valid indications of activity against *E. vermicularis* in man and to demonstrate substances worthy of clinical trials.

Material and Method

White mice 11–12 weeks old showing ova of *Aspiculuris* in the faeces were segregated and used for drug-testing. Necropsy of untreated mice showed a range of 2–120 worms per mouse. Because of the relatively small number (10–20) of mice that could be used in each test it was considered that this range in numbers of worms was too large to warrant valid statistical deductions to be drawn on the basis of reduction in worm numbers following treatment. Therefore the degree of activity of a drug was estimated in relation to the dose required to clear the worms from all or a proportion of the mice treated. The drugs were given orally by stomach tube as a solution or suspension in water or liquid paraffin. The animals were dosed either once or twice daily for five consecutive days. According to the availability of infected mice, 10–20 animals were used for each test. Faecal examinations were made at six days and necropsy at 12 days after completion of treatment. In some instances necropsy was carried out at six days after treatment without prior faecal examination.

To facilitate worm counts the rectum and caecum of each mouse were removed at necropsy and placed in Bouin's fixative. Material fixed in this way could be stored and examined when convenient. At examination this portion of the gut was slit open under water and the contents were removed gently with a camel-hair brush. The inside of the examination dish was painted black, and the worms, now stained bright yellow, were easily seen and counted against this background.

Results

Table I shows the relative efficiency of a number of reputed oxyuricides in clearing mice of *Aspiculuris*. None of the drugs used, except perhaps oil of garlic, was particularly toxic* at the dosages employed, and only two, gentian violet and piperazine hydrate, produced any marked worm clearance. In seven other instances partial clearances were obtained, but four of these (Nos. 4, 6, 10, and 13)

* All mice on test had been exposed to infection with *Schistosoma mansoni*. A proportion of the mouse mortality would result from this.

TABLE I.—*Showing the Relative Efficiency of Several Reputed Oxyuricides and Some Related Compounds in Clearing Mice of Naturally Acquired Threadworm (Aspiculuris tetraptera) Infections*

No.	Drug	Oral Dose (mg./kg.)	No. of Doses Daily	Total Dose (mg./kg.)	Mice Surviving at Necropsy	Days After Treatment	% Mice Cleared of Worms	Average No. of Worms per Mouse	Range in No. of Worms	Drug Efficiency Rating
1	Gentian violet	90	1	450	16/20	12	80	7	2–11	+++
2	Piperazine hydrate	400	1	2,000	13/13	12	100	0	—	++++
3	N-carbethoxypiperazine hydrochloride	400	1	2,000	12/13	12	0	44	8–183	–
4	1-Diethylcarbamyl 4-methylpiperazine citrate ("banocide," "hetrazan") syrup	500	1	2,500	9/10	12	10	24	2–77	–
	" " " powder	500	1	2,500	9/12	12	0	37	4–152	–
5	N-*iso*amylcarbaminic acid-3-methyl-6-*iso*propyl phenyl ester ("egressin")	200	2	2,000	9/12	6	0	68	11–158	–
6	Aluminium 8-hydroxyquinoline ("nyxolan") syrup	60	2	600	10/10	12	10	37	2–94	–
7	Diphenan	700	1	3,500	18/20	12	0	101	18–154	–
8	Quinoxaline	150	2	1,500	11/12	6	0	94	37–187	–
9	Mepacrine	50	2	500	12/12	6	25	29	3–60	+
10	Phenothiazine	100	1	500	12/13	12	8	62	15–114	–
11	Santonin	200	1	1,000	9/10	12	20	38	3–107	±
12	Hexylresorcinol	20	1	100	9/12	12	0	67	2–125	–
		10	1	50	12/13	12	40	59	16–163	+
13	Dried garlic ("allisatin")	200	2	2,000	8/10	12	10	83	53–165	–
14	Oil of garlic	½ minim per kg.	2	2½ minims per kg.	6/10	12	0	45	5–121	–
15	Allyl sulphide	"	2	"	8/10	12	0	61	2–121	–
16	Liquid paraffin	10 ml. per kg.	2	100 ml. per kg.	5/5	12	0	56	20–72	–

TABLE II.—*Showing the Graded Dosage Effect of Gentian Violet and Piperazine Hydrate in Clearance of Aspiculuris tetraptera from Naturally Infected Mice*

Drug	Oral Dose (mg./kg.)	No. Doses Daily	Total Dose (mg./kg.)	Mice Surviving at Necropsy	Days After Treatment	% Mice Cleared of Worms	Average No. of Worms per Mouse	Range in No. of Worms	Drug Efficiency Rating
Gentian violet	100	1	500	5/10	12	100	0	—	++++
	90	1	450	16/20	12	80	7·0	2–11	+++
	50	1	250	10/10	12	100	0	—	++++
	25	1	125	10/10	12	0	31·0	2–61	–
Piperazine hydrate	400	1	2,000	13/13	12	100	0	—	++++
	200	1	1,000	10/13	12	90	0·1	0–1	+++
	100	1	500	13/13	12	62	3·0	1–8	++
	50	1	250	12/13	12	31	40·0	2–212	+

were of 10% or less, and can be ignored. Other clearances —hexylresorcinol (40%), mepacrine (25%), and santonin (20%)—were not convincing. In the case of hexylresorcinol the 40% clearance was obtained with 10 mg./kg. unit dose, but no clearance resulted when the dose was doubled. Obviously some spontaneous clearance may occur, and unless reasonably uniform results are produced in repeated tests isolated successes must be disregarded.

The clearance rates obtained with gentian violet and piperazine were further investigated. The results of these further tests, together with the original ones, are given in Table II. It will be seen that gentian violet gave a ++++ rate at 50 mg./kg. unit dose, but failed to clear at 25 mg./kg. Piperazine hydrate gave a good response at 400 and 200 mg./kg. unit dose, and at most dose levels the numbers of worms left were very small. In the piperazine 50 mg./kg. group one mouse had 212 worms, whilst the average for the remaining seven positives was only 15. At the 200 mg./kg. level only one mouse remained infected, and this had only one worm, whilst the scanty worm burden remaining at the 100 mg./kg. dose level is perhaps additional evidence of drug activity.

It may be concluded that, in terms of dose/weight ratio, gentian violet is rather more efficient in clearing mice of *A. tetraptera* than is piperazine hydrate, but, nevertheless, piperazine is highly promising and is worthy of clinical trial. The rate at which the intestinal contents move in the mouse is very high compared with that in man, and it is conceivable that in the human subject the piperazine may be absorbed or destroyed before it reaches the worms.

Since this work was completed, clinical trials of piperazine hydrate, gentian violet, and diphenan have been concluded (White and Standen, 1953). The activity of piperazine hydrate and gentian violet against *Aspiculuris* in the mouse is confirmed against *Enterobius vermicularis* in children, whilst diphenan, inactive against *Aspiculuris*, was similarly shown to be of no value in the treatment of human oxyuriasis. The comparative evidence so obtained justifies the use of *Aspiculuris* in a laboratory screen against threadworm infestation.

Summary

Aspiculuris tetraptera, threadworm of the mouse, was used to test the efficacy of reputed oxyuricides. Of these, only gentian violet and piperazine hydrate cleared the mice of worms.

Drug-testing against *Aspiculuris tetraptera* in the mouse is of considerable value in establishing the efficiency of oxyuricides prior to clinical trial.

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Regulations which came into effect on September 1 control the manufacture of aureomycin. When it is intended for parenteral injection it may not be manufactured for sale except under licence and in conformity with prescribed conditions as to strength, quality, and purity. The regulations are entitled the Therapeutic Substances Amendment Regulations, 1953.

VAGINAL ULCERATION DUE TO POTASSIUM PERMANGANATE

BY

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Over 100 cases of vaginal ulceration following the insertion of potassium permanganate tablets for the purpose of procuring an abortion have been described since the first account of this condition by Lacassagne and Friess in 1932. Voron, Rochet, and Contamin (1935) reported a case in which severe arterial bleeding resulted from the ulceration in the vagina. Shull (1941), among 17 patients with a similar condition, followed up four in whom pregnancy was confirmed; only one patient miscarried. The largest series has so far been described by McDonough (1945). Of 65 patients, 34 required packing of the vagina to control the bleeding and 12 needed transfusion. In 40 patients pregnancy was confirmed; six miscarried, and one was delivered by caesarean section on account of scarring following the vaginal ulceration. Blondin, Benassy, and Masse (1948) added two more cases. Jetter and Hunter (1949) described the case of a woman who died after using a douche of saturated permanganate solution containing a total of over 7 g.

The first account in the British literature was reported by Miller (1951), who described 10 cases. In some of these he found ligation of arterial bleeding points in the base of the ulcer necessary, and formed the opinion that pregnancy remained undisturbed unless the tablets were introduced into the region of the cervix. Henderson and Watt (1951) reported that they had seen cases for many years, and caesarean section had been necessary in three on account of scarring of the vagina.

The following four cases seen at St. Bartholomew's and the London Hospitals are described to draw further attention to the widespread practice of using potassium permanganate, especially in tablet form, as an "abortifacient," and to deprecate the method as an effective means of terminating pregnancy. In the first case, seen in the gynaecological department at St. Bartholomew's Hospital, although typical vaginal ulceration was present the use of potassium permanganate tablets inserted direct into the vagina was not established. One of the other three cases was seen in the gynaecological department of the London Hospital, and a history of using tablets followed by vaginal bleeding was obtained, but no vaginal ulceration was seen. The remaining two patients first attended at the Whitechapel Clinic of the London Hospital. In both these cases the diagnosis was fully established and photographic records were made.

Case 1

A 3-para aged 38 attended St. Bartholomew's Hospital on November 25, 1950, with vaginal bleeding in pregnancy. Her last regular period had begun 23 weeks before attending. Vaginal bleeding, she stated, had occurred two weeks later, and had continued intermittently until a heavy loss a week previously, after which it had ceased. She admitted using a douche made up with potassium permanganate tablets, but denied inserting any of these tablets directly into the vagina.

Examination showed a healthy woman; the uterus was enlarged to the size of 24 weeks' gestation, and the foetal heart was audible. In the vagina were two apposition ulcers, one in the anterior and one in the posterior wall, about 5 cm. from the introitus. A grey slough was present in the base of each, and both bled readily to the touch. Routine investigations in the special treatment centre, including dark-ground examinations, all proved negative. During the next two weeks healing of the ulcers took place with no scarring, and arrangements for antenatal care were made, but the patient subsequently defaulted.

Case 2

A single nulliparous girl aged 16 was admitted to the London Hospital on January 19, 1952, on account of vaginal bleeding in pregnancy. Her last regular period had begun 22 weeks previously. Twenty-four hours before admission, she stated, she had inserted two tablets of potassium permanganate into the vagina. A few hours later she experienced slight pain in the lower abdomen associated with bright vaginal bleeding.

Examination showed a healthy girl with the uterus enlarged to the size of 22 weeks' gestation. No vaginal ulceration was seen on examination with a speculum. Pregnancy was confirmed by an Aschheim–Zondek test, and the patient gave birth to a live premature infant 12 weeks later.

Case 3

A single nulliparous woman aged 22 attended the London Hospital on February 14, 1952, with a history of pain and swelling of the vulva for two days associated with dysuria. Her last regular period had begun five weeks previously; the normal cycle was 28 days.

Examination showed two shallow apposition ulcers with greyish bases 1.5 cm. in diameter on the inner aspect of the labia minora. Black debris which was scattered elsewhere over the vulva consisted of manganese dioxide produced by the breakdown of potassium permanganate. On passing a speculum another two apposition ulcers, circular and deeper than those on the vulva, were seen in the anterior and posterior vaginal walls just below the level of the cervix, with a disintegrating tablet *in situ*, and further brownish-black debris was scattered over the vaginal wall. All routine investigations, including dark-ground examination of the ulcers, proved negative.

It was only on further questioning that the patient gave the following details. Eight days before attending, fearing she might have conceived, she had inserted tablets into the vagina just before her next period was due. She had worn a sanitary pad to retain them. Heavy vaginal bleeding had ensued. It is assumed that the vulval ulceration had been caused by one of the tablets slipping down between the labia shortly after insertion. On her next attendance the patient brought for inspection a tablet similar to those she had inserted. This was analysed and found to be a compressed tablet of 5 gr. (325 mg.) of potassium permanganate.

During the next four weeks the ulcers healed completely without residual scarring. The cervix became softened and the uterus enlarged; three weeks after the patient first attended an Aschheim–Zondek test confirmed that she was pregnant.

Case 4

A single nulliparous woman aged 28 attended the London Hospital on May 13, 1952, with a history of brown vaginal discharge. The last menstrual period had been nine weeks previously. Her normal menstrual cycle was 28 days, and, believing herself to be pregnant, she had inserted three tablets of potassium permanganate into the vagina three days before

attending. Slight bleeding began the following day. She produced a bottle of 100 2-gr. (130-mg.) tablets of potassium permanganate which she had obtained from a chemist.

Examination of the vagina with a speculum revealed a deep circular ulcer 1.5 cm. in diameter on the portio vaginalis of the cervix to the right of the external os. A similar ulcer lay in apposition on the right vaginal wall (see accompanying photograph). Much black debris was present in the vagina. The cervix was soft, and the uterus enlarged to correspond with the period of amenorrhoea. Routine investigations, including dark-ground examinations of the ulcers, were negative. The Aschheim-Zondek test was positive. Analysis of one of the tablets confirmed that it was potassium permanganate.

Photograph showing appearance of cervix and posterior vaginal fornix in Case 4.

At subsequent attendances the ulcers were seen to heal slowly and spontaneously, and after three weeks' observation no trace of them, and no scarring, remained. The patient miscarried one month later as a result of interference of a different kind.

Discussion

Of the four cases described, three were found to have the characteristic apposition ulcers produced by potassium permanganate in high local concentration. Three patients gave a history of inserting tablets to achieve abortion; the remaining one admitted only using a solution of tablets in a douche, although typical circular vaginal ulcers were found. Bleeding occurred in all four cases, although in none was it enough to warrant the measures described by other writers. Abortion did not occur as a result of the use of tablets in any of the patients. This conforms to the experience of others that the agent is not usually an effective abortifacient. It should be noted that two patients first attended at a gynaecological out-patient department, and two at a special treatment centre. A history of pregnancy may not be forthcoming, the irregular bleeding being the only complaint. The use of tablets may not be admitted initially by the patient. Therefore correct diagnosis of the condition may rest upon finding the characteristic circular apposition ulcers in the lower genital tract, with the remains of a tablet or the brownish-black debris of manganese dioxide still *in situ*.

The similarity of these ulcers to primary chancres in the male was pointed out by Blondin *et al.*, who described the practice of certain legionaries who malingered by inserting a tablet of potassium permanganate under the prepuce. A provisional diagnosis of primary syphilis in women with lesions suggesting contact chancres is therefore likely to be made until full investigations, including dark-ground examination and serological tests, fail to confirm the diagnosis. It is then that further questioning may reveal the true history of the use of potassium permanganate tablets as an abortifacient.

2-gr. and 5-gr. (130-mg. and 325-mg.) tablets of potassium permanganate are readily obtainable at chemists. There is no restriction on their sale.

Summary

Four cases of bleeding following the insertion of potassium permanganate into the vagina in pregnancy are described.

The use of this chemical in tablet form was confirmed in three cases.

The typical ulceration produced is illustrated by a photograph.

The tablets used in two cases were subjected to chemical analysis.

The possible confusion of the lesion with primary chancres, especially in patients who conceal the true history and first attend at special treatment centres, is pointed out.

The common use by women of potassium permanganate in tablet form for procuring abortion and the ease with which it may be obtained for this purpose are stressed. It does not appear to be an effective abortifacient.

ADDENDUM.—Since preparing this report one of us (E. A. J. A.) has seen a fifth patient, in whom very heavy bleeding was caused by the vaginal ulceration. A single girl aged 19, who subsequently admitted inserting tablets of potassium permanganate into the vagina for fear of pregnancy, was admitted on account of a sudden profuse haemorrhage. After half a pint (285 ml.) of fresh blood clot had been removed from the vagina, ulcers were seen on the anterior and posterior walls. The anterior ulcer had eroded the wall of a large artery, which was bleeding freely. Ligation of the vessel was necessary.

Our thanks are due to Dr. Ambrose King, senior physician at the Whitechapel Clinic of the London Hospital; to Dr. Eva Gallagher, who assisted in the follow-up of cases in the Whitechapel Clinic; and to the photographic department of the London Hospital. Permission to describe their cases is gratefully acknowledged to Mr. Wilfred Shaw and Mr. Donald Fraser at St. Bartholomew's Hospital, and to Mr. Alan Brews at the London Hospital.

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Launching the autumn recruiting campaign for the National Hospital Service Reserve last month, the Minister of Health, Mr. Iain Macleod, said that in order to be ready to meet the demands of war the Reserve must increase its present strength of 30,000 volunteers to 100,000. He hoped that the new drive for recruits would carry the total well on its way to this target. The Reserve had its role in peacetime too, in dealing with the emergencies of everyday life. "We have had some pretty grim reminders of this in Lynmouth and the East Coast floods and two terrible railway disasters within the last twelve months," he said. "It may not be generally realized," he continued, "that each year there are over one million serious accidents in our homes—serious enough, that is, to require treatment in hospital—and that another 200,000 injuries occur on the roads. With these facts in mind I ask myself: Should not every man and woman have some training in first-aid and simple home-nursing, and would not women gain in confidence and competence if they added practical knowledge of first-aid and simple nursing to their many other accomplishments? The chances are that each one of us some time in our lives will be confronted with a serious accident or injury in our homes, at work, on holiday, or on the roads. We all dread the possibility, but knowledge and training would take the dread out of such occasions, substituting confidence and competence for fear and futility."

PREGNANCY AND GAUCHER'S DISEASE

BY

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Gaucher's disease is a rare condition affecting the reticulo-endothelial system, which is loaded with a complex lipo-protein (kerasin, a cerebroside) not normally found in the body. Clinically this condition is known to be characterized by an enlargement of the spleen, sometimes reaching to enormous dimensions, a much less marked hepatomegaly, moderate anaemia, leucopenia, and thrombocytopenia, with a tendency to bleeding, skeletal changes, a brownish pigmentation of the skin, and frequently a peculiar yellowish thickening of the conjunctiva (pinguicula). Most of the above manifestations are due to an invasion of the spleen, liver, and bone marrow by large histiocytic elements with a foamy cytoplasm charged with kerasin, which are termed Gaucher's cells and are pathognomonic of the disease.

The condition has a familial tendency and may appear in infancy and childhood, but diagnosis is usually arrived at in the adult. Females are more often affected than males, and the disease has a predilection for the Jewish race.

We were repeatedly confronted with the problem of management of pregnancy in Jewish patients affected by Gaucher's disease, and, surprisingly enough, could find no data in the available literature on this subject. Indeed, the only reference to the influence of the disease on the female genital functions concerns the frequent occurrence of menorrhagia (Brill and Mandlebaum, 1913). The haemorrhagic tendencies, the anaemia, the splenomegaly, the destructive changes in the bones, and the poor general condition of these patients may lead obstetricians to consider the interruption of pregnancy. We felt, therefore, that a report of our experience of Gaucher's disease complicated by pregnancy might be helpful for an evaluation of the risks involved.

Material

The present study is that of a group of seven Jewish women of Eastern European extraction affected by Gaucher's disease in whom the course of 13 pregnancies was recorded (Table I). Nine were deliveries at term, resulting in nine living offspring, and four pregnancies were interrupted. One of the patients had a twin pregnancy, and on delivery bore one living child, the other being stillborn. The pregnancies occurred between the ages of 21 and 36 years. The first pregnancies were preceded by a marriage interval of 0.5–1.5 years in four cases (Cases 2, 3, 5, and 7), whilst in three cases conception was preceded by a period of sterility, involuntary in one case (Case 6) and voluntary in two cases (Cases 1 and 4).

TABLE I.—*Data on Pregnancies in Seven Women Affected by Gaucher's Disease, in Relation to Establishment of the Diagnosis*

Case No.	Age at First Examination	Age at Appearance of Symptoms	Age when Disease Diagnosed	Age at Marriage	No. of Pregnancies	Age at Pregnancy				Full-term Delivery	Children Alive	Therapeutic Abortions
						1st	2nd	3rd	4th			
1	34	32	34	21	3	30	34	36	—	2	2	1
2	26	24	26	22	2	23	25	—	—	1	1	1
3	33	18	28	26	1	26	—	—	—	1*	1†	—
4	29	10	24	20	1	24	—	—	—	1	1	—
5	32	31	32	26	1	27	—	—	—	1	1	—
6	25	?	25	19	4	25	27	29	32	2	2	2
7	12	12	16	20	1	21	—	—	—	1	1	—

* Twins. † One was a stillbirth (cerebral haemorrhage).

Parity.—Four out of seven patients had only one pregnancy, which ended with a full-term delivery (Cases 3, 4, 5, and 7), while three others had respectively three, two, and four pregnancies (Cases 1, 2, and 6). Case 1 had two full-term deliveries and one artificially induced abortion. Case 2 had one full-term pregnancy and one artificially induced abortion. Case 6 had two full-term pregnancies and two induced abortions (the abortions in all cases having been performed because of Gaucher's disease). The patients who conceived only once had been discouraged by their medical advisers from venturing upon further pregnancies. It should be mentioned that the current medical opinion among the physicians of Israel is that pregnancy involves increased risks for the patient affected by Gaucher's disease, and that the majority of full-term pregnancies reported in the present paper occurred, therefore, before the diagnosis of the disease was established.

In all cases reported (Table I) the diagnosis was based on the absolute criterion of finding Gaucher's cells in the bone marrow or spleen. The clinical manifestations and relevant laboratory findings are given in Table II.

Menstrual History.—In three of the seven cases periods of menorrhagia were recorded (Table II). In none was the increased blood loss during the menstrual periods severe enough to require special treatment. Menstruation occurred regularly during the observation periods of two to seven years. In Case 4 a short period of amenorrhoea occurred, lasting three months. Cases 2 and 6 became pregnant while suffering from menorrhagia, indicating that this increased menstrual flow was not associated with failure to ovulate.

Influence of Gaucher's Disease on Course of Pregnancy

In this series there was no case of spontaneous abortion or premature labour. The course of pregnancy was not complicated by the toxaemias or by haemorrhagic accidents. It should be noted that the enormous spleen typical of the disease does not interfere with the normal increase in size of the gravid uterus. This was our experience with two cases (Nos. 1 and 6) in which no distress resulted from the pressure of the uterus on the enlarged spleen and liver. All the babies delivered at full term were normally developed and their birth weights within normal range. No case of foetal death *in utero* occurred. In Case 3, a twin pregnancy, one foetus died during delivery, and post-mortem examination revealed a cerebral haemorrhage. The course of labour in all cases was uneventful. The third stage was not complicated by haemorrhage of more than an average amount, in spite of the known tendency to bleeding found in these patients. Lactation was normal in all but one case.

Influence of Pregnancy on Gaucher's Disease

It was our experience that pregnancy did not adversely affect the course of Gaucher's disease. On the contrary, in at least two patients there was an increased feeling of well-being during pregnancy (Cases 4 and 6). That in these two cases the diagnosis of Gaucher's disease was made during pregnancy was not due to any deterioration in the condition of the patient but to the finding of splenomegaly on

TABLE II.—*Clinical Symptoms and Relevant Laboratory Findings in Seven Patients Affected by Gaucher's Disease*

Case No.	Spleen	Liver	Bones	Pigmentation	Pinguicula	Haemorrhages (At Time of First Examination and in Previous History)	Bone Marrow	Splenic Puncture	Blood Picture	Blood Cholesterol (mg./100 ml.)	Remarks
1	Hard. Enlarged to 2 fingers above iliac crest	4 fingers below costal margin	No changes	Dark pigmentation of exposed parts and of oral mucous membranes	Bilateral	Subungual. Ano-rectal. Menorrhagia	Gaucher's cells	—	R.B.C. 3,600,000. W.B.C. 3,600. Hb 10 g./100 ml. Thrombocytes 110,000	150–190	2 weeks after second delivery
2	Hard. Enlarged to 2 fingers below iliac crests	Hard. 3 fingers below costal margin	"Erlenmeyer flasks" in both femurs	Dark pigmentation of face, especially forehead and cheeks	—	Menorrhagia	,,	—	R.B.C. 3,400,000. W.B.C. 4,200. Hb 10 g./100 ml. Thrombocytes 90,000	130–160	
3	Hard. Level with iliac crests	Hard. Reaches to iliac crests	"Erlenmeyer flasks" in both femurs*	Pigmentation of face, especially forehead	Bilateral	Subcutaneous	,,	Gaucher's cells	R.B.C. 4,200,000. W.B.C. 2,100. Hb 12 g./100 ml. Thrombocytes 280,000	165	
4	Hard. Reaches the symphysis pubis	Hard. 2 fingers below costal margin	No changes	Yellowish, of the face	—	Epistaxis	,,	,,	R.B.C. 3,200,000. W.B.C. 2,600. Hb 9 g./100 ml. Thrombocytes 60,000	90–100	
5	2 fingers above iliac crests	Not enlarged	"Erlenmeyer flasks" in both femurs	—	—	—	—	,,	R.B.C. 4,180,000. W.B.C. 3,800. Hb 12 g./100 ml.	—	
6	Hard. Reaches iliac crest	Hard. Reaches umbilicus	No changes	Yellowish, of the face	Right eye	Menorrhagia. Epistaxis. Dental. Subcutaneous	Gaucher's cells	—	R.B.C. 2,700,000. W.B.C. 3,200. Hb 9·8 g./100 ml. Thrombocytes 85,000	100–138	7 months pregnant
7	Hard. 4 fingers below costal margin	2 fingers below costal margin	No changes	—	—	—	,,	—	R.B.C. 3,950,000. W.B.C. 2,800. Hb 14·8 g./100 ml. Thrombocytes 105,000	—	

* Some impairment of movements and muscular atrophy.

routine abdominal examination. The major manifestations of Gaucher's disease did not appear to be aggravated during pregnancy. No changes were noted in the size of the spleen or liver. Despite considerable thrombocytopenia (in Case 4 and in the first and second pregnancies in Case 6) no aggravation of the haemorrhagic tendency was observed. In Case 1 severe bleeding from the anorectal mucosa, a condition antedating the third pregnancy, continued during the first two months and went on unabated after the pregnancy had been interrupted. Severe skeletal changes, accompanied by impairment of function in the lower extremities, preceded pregnancy in Case 3. No further anatomical or functional damage was wrought by the pregnancy. The general impression received during the relatively short period of observation was that pregnancy or repeated pregnancies have no adverse effect upon the disease.

Discussion

The course of Gaucher's disease is a chronic one interrupted by infrequent exacerbations characterized by haemorrhagic episodes, bone pains, and a general deterioration in the patient's condition. Thannhauser (1950) states that "in the interval (between individual flare-ups), which often lasts 10 years or more, there are no complaints and no disturbances of important functions. The patient may lead a normal life and even perform hard work. . . ." Life expectancy of these patients seems to be only slightly affected, especially when symptoms become manifest during or later than the third decade (Thannhauser, 1950).

In our opinion, women affected by the disease should not be deprived of the chance of becoming mothers if a negative answer can be given to the following two questions. (1) Does pregnancy endanger the life of the woman? (2) Does the disease affect the offspring?

This study of nine full-term pregnancies in seven patients leads us to believe that childbirth does not exert any deleterious effect, either immediate or remote, upon the woman suffering from Gaucher's disease. In fact, in every case in this series there was a comfortable pregnancy, followed by a successful normal full-term delivery. It is especially important to observe that haemorrhagic complications, which could be expected in Gaucher's disease, did not in fact occur. In Case 6 we had the opportunity of studying the patient over a period of seven years, throughout the course of four pregnancies, and no deterioration in her condition was observed.

Concerning the fate of the offspring, our short period of observation allows only limited conclusions. All infants born in our series were normal at birth and subsequently showed normal development. None showed any manifestation of Gaucher's disease. No absolute evidence that the disease is hereditary has been claimed in the literature on the subject, and the chances of the child becoming affected by the same condition are negligible.

It seems justifiable to draw the conclusion that women affected by Gaucher's disease should not be denied motherhood. No justification for the interruption of pregnancy in patients affected by the disease was found in the present study.

Summary

The course of 13 pregnancies in seven patients affected by Gaucher's disease has been studied. Nine pregnancies proceeded to full-term deliveries and four were interrupted during the first trimester.

The course of the nine pregnancies which continued to term was uneventful, and they terminated in normal deliveries of apparently healthy babies.

Four pregnancies were interrupted because of the prevalent opinion that pregnancy involves serious risks for the woman affected by Gaucher's disease.

The effects upon each other of pregnancy and Gaucher's disease are discussed and the conclusions drawn that conception in women affected by the disease should not be discouraged, and that interruption of pregnancy in this condition is not justified.

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USE OF THE ELECTRODERMATOME, WITH SPECIAL REFERENCE TO ITS VALUE IN SERIOUS BURNS

BY

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This article is based on experience with the electrodermatome during the past year at the Basingstoke Plastic Centre. Our experience in plastic and general surgery confirms the view widely held in America that in ease and reliability of cutting grafts of varying sizes and depth the electrodermatome presents an advance over other graft-cutting instruments. The graft-cutting instruments hitherto available have been the Thiersch razor, the Blair blade, the Humby knife, and the Paget dermatome. Of these the Humby knife has the widest range of general usefulness and needs the least experience for reliable results. The razor is, of course, in all respects inferior to the Blair blade, but even with the Blair blade in the most expert hands it is not possible with certainty to cut areas of graft from the thigh (the most common donor site) of more than 8 to 10 by 3 to 4 in. (20 to 25 by 7.5 to 10 cm.); the graft can be cut of uniform thickness only if it is very thin. Irregularities in thickness leading to poor donor-site scars are common. With the Humby knife grafts of 10 by 4 in. (25 by 10 cm.) can be cut with some practice. It has the added advantage of making possible grafts of medium thickness in depth; but again thickness of graft tends to vary. The Paget dermatome cuts an area of up to 8 by 4 in. (20 by 10 cm.). This instrument has been of great value in certain definitive repairs of the hand and elsewhere, but the donor-site scars are liable to keloid formation; it is a time-consuming method, and there is often trouble with the dermatome cement. Furthermore, in addition to the limitation of length it is not possible to cut thin split-skin grafts reliably with it.

There are many repairs which properly belong to the field of general surgery but which are still often referred to plastic centres simply because of the technical difficulty which current grafting instruments present to surgeons. Early experience in watching the use of the electrodermatome in a general surgical service (at the Brooke Army Hospital, San Antonio, Texas) convinced one of us that the electrodermatome could be of value in this way, as well as being an advance on other grafting instruments in the ease, speed, and reliability with which extensive reasonably thin split-skin grafts could be cut from a variety of donor sites in patients with serious deep burns.

The Instrument

The electrodermatome was introduced in the United States after the last war. It is an electrically powered instrument in which a rapidly oscillating blade placed horizontally cuts against a lower fixed bar. The thickness of the graft can be regulated by adjusting the two micrometer screws which carry a vertically adjustable bar immediately above the knife edge. Grafts from 0.015 to 0.055 in. (0.038 to 0.138 cm.) can be cut. The maximum width of graft, which is 3 in. (7.5 cm.), can be reduced as required by a third screw which operates a pair of width guides against which the blade cuts. The length of graft is limited only by the extent of the donor area. The small electric motor is encased in metal to ensure its being spark-proof. It is connected to the instrument by means of a flexible drive shaft, and is operated on 10 volts A.C. or D.C. by a foot switch controlled by the surgeon. The knife blade is slotted into the instrument much as a razor blade into a razor, and is held there by three screws which are tightened by a spanner. We have found it possible to get good use out of blades which have been sharpened two or three times, although this is contrary to the manufacturers' experience. One blade will remain sharp during the cutting of skin from most of a thigh.

For sterilization, the dermatome, flexible shaft, and spanner are autoclaved; the blades are cold-sterilized. The motor, which does not enter the sterile field, must not be autoclaved. It is simply cleaned with a damp cloth.

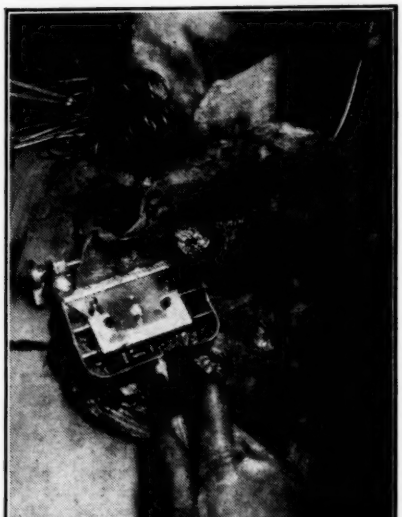

Fig. 1.—Early excision of sloughs with the electrodermatome. The instrument is run once or twice rapidly over the burnt area (in this case on the fifth day).

Operation of the Electrodermatome

An adequate or the best available site is selected; it may be thighs, buttocks, legs, arms, chest, abdomen, or back—that is, any area except head, neck, hands, and feet. The skin of the donor site is covered with a thin coating of mineral oil such as sterile liquid paraffin. It is put on a slight stretch by the surgeon's free hand, placed behind the area from which the graft is to be cut. The dermatome is then placed with its undersurface flat against the skin. While firm pressure is maintained on it the instrument is moved slowly and steadily forward. An assistant grasps the cut edge of the skin graft with a pair of haemostats placed on each corner as the graft presents above the cutting blade, and slight tension is maintained by him on the graft. When the necessary length of graft has been cut the front of the instrument is directed upwards to sever the attachment of graft to the donor site.

Applications of the Electrodermatome

1. *In Burns.—Graft cutting:*—The special value of the instrument is the ease and speed with which extensive areas of graft can be cut even by those with little experience in its use. This saving of time can be of great importance during an operation in the second week in cases of serious

FIG. 2.—Grafting of extensive varicose ulcers. The pre-operative photograph of an elderly patient who had been in hospital for two years on account of circumferential bilateral extensive ulcers.

burns. An additional advantage is the thinness of the skin. There need therefore be less blood loss during the operation, and these donor sites can be soon "milked" again when necessary. Nor are they likely to give rise to hypertrophic and unsightly scars so often caused by the Paget dermatome. The instrument is also of value in definitive repairs for burn deformities, when medium or thicker-quality skin may be needed. *Slough removal*:—The electrodermatome is also in our experience the quickest and least haemorrhagic of methods for the early removal of some sloughs (Fig. 1). In a matter of a few minutes very extensive areas can be cleared. The dermatome can be run over the same area more than once until an unquestionably viable bed is exposed. In some circumferential burns of the trunk of uniform depth it can happen that front and flank skin has been lost to full-thickness depth while the thicker lumbar skin still has viable dermal elements. These if covered by homogenous grafts, after removal of the coagulated superficial sloughs by the electrodermatome, may heal permanently without the breakdown which appears in the homogenous grafts placed on subcutaneous beds in the same patient at the same time. This is presumably due to a creeping substitution of the homogenous cells by autogenous epithelial elements in the surviving dermis.

FIG. 3.—Post-operative photograph of the same case as Fig. 2. Four months after radical excision of ulcer, scarred epithelium, and fibrous tissue. Areas covered with thin split-skin grafts cut by the electrodermatome from the thighs.

2. *Avulsion Flaps.*—The instrument has potential value in the treatment of patients who have severe shearing injuries with avulsion of skin and subcutaneous tissue from their underlying beds. Much of these flaps apparently viable at first is later lost by thrombosis or other cause. By use of the electrodermatome at primary operation the superficial layer of epidermis could be easily and quickly removed as thin grafts from those areas of the flaps whose future viability was suspect. These grafts could be stored at 4° C. for subsequent use (leaving the flap to declare itself) or applied at primary operation after excision of the flaps.

3. *Other Soft-tissue Injuries and Surgical Problems.*—The instrument is of most value where extensive uniform-depth grafts are needed, and especially when it is desirable to save time and limit blood loss. It has therefore a role in any major soft-tissue loss. Its value in the reparative stage of radical mastectomy operation is the ease with which the adjacent trunk skin can be cut to cover residual defects.

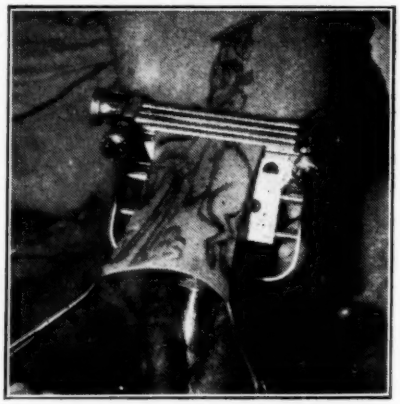

FIG. 4.—Use of the electrodermatome for removal or obscuration of extensive tattoo designs.

4. *Varicose Ulcers.*—Certain extensive varicose and gravitational ulcers, such as the circumferential ulcers depicted in Fig. 2, need a repair by very extensive grafts (Fig. 3) of a skin of reasonable quality. Many of these patients are elderly, for whom it is undesirable to prolong the time of operation. We have used the electrodermatome to provide extensive grafts quickly and of a quality which holds a suture securely.

5. *Lymphoedema.*—In cases chosen for treatment by circumferential excision of skin and fat down to fascia and muscle, the electrodermatome is the most efficient method of first removing skin grafts from the skin of affected areas to be discarded. These grafts can be used to cover the raw areas established by the excision.

6. *Tattoo Marks and Facial Acne.*—The electrodermatome will rapidly efface the design of a tattoo mark (Fig. 4). It may not remove the staining completely if the tattoo is deep, but the result is generally a very effective obscuration of a design which has often long since ceased to please the patient. The instrument has also been used to remove severe and extensive acne of the face.

Summary

Attention is drawn to the value of the electrodermatome, both in general and in plastic surgery.

It is suggested that the expense of this rather costly instrument would be justified for any large surgical service. Our reasons for this belief are the greatly increased ease and speed with which extensive grafts of any thickness may be cut by it with little experience. We believe the instrument represents a further stage in the simplification of graft-cutting techniques, and one that is likely to increase the scope of the reparative work which can be retained in general surgical services.

We have found it of special value in cutting extensive grafts for severe burns, especially when the usual donor sites are not available.

It has also proved a most efficient agent for the removal of burn sloughs from the trunk and limbs.

As a graft-cutting instrument it has a number of other valuable uses, especially in the surgery of trauma.

A new low record for accidents in the mines was established in 1951, according to the annual report of H.M. Chief Inspector of Mines. Persons killed totalled 487, and 1,942 were seriously injured. In comparison with 1950 these were 6 fewer killed and 78 fewer injured. These record figures were attained in spite of the serious disaster at Easington Colliery, in Durham, which caused the death, directly or indirectly, of 83 people.

Medical Memorandum

Prolapse of the Urethra in Young Girls

Prolapse of the urethral mucosa in the adult woman is well recognized, but it is not so well appreciated that the condition occurs in young girls. Keefe (1917), in a study of the recorded cases, found that 60% of the patients were children, 28% were women over 40 years of age, and the remaining 12% were between 15 and 40 years of age.

Case Report

A 7-year-old girl was brought to hospital in January, 1952, on account of a blood-stained discharge which soiled her clothes. This "spotting" was of three days' duration and was accompanied by some pain in the urethral region on micturition.

On examination an inflamed ring of tissue surrounding the urethral opening was seen. No other abnormality was found. She was admitted to hospital a few days later. Under general anaesthesia the vulva was more carefully examined. The urethral meatus was surrounded by an oedematous and bruised ring of urethral mucosa (see photograph). No abnormality was observed in the vagina or of the cervix. Cystoscopy was carried out, but no abnormality was seen.

Photograph showing inflamed oedematous urethral meatus.

The prolapsed mucosa was excised circumferentially and the cut end of the urethra sutured to the skin surrounding the meatus by a few interrupted catgut stitches. Convalescence was uneventful, and the patient was discharged well and free from symptoms on the eleventh day.

Section of the excised tissue showed a covering of transitional epithelium, which was shed in places, over an engorged submucosa containing round-cell infiltration.

Aetiology

The condition may occur at any age. It is reported that the youngest patient was 5 days and the oldest 92 years (Epsteen and Strauss, 1937). Hepburn (1920) believes that the supporting structures around the bladder neck are poor in these cases, and that straining produces a partial herniation of the bladder (and urethral mucosa with it) through these poor supporting structures. Certainly the condition has been observed following severe coughing and straining at stool. Keefe (1917) suggests that excessive force by the detrusor muscle of the bladder causes prolapse of a loose mucosa of the urethra. Chute (1925) reported three cases of partial prolapse of the urethral mucosa associated with malignant disease of the bladder and vesical tenesmus. It would appear that, provided the urethral mucosa is only loosely supported, an increased downward pressure, whether supplied by the vesical detrusor muscle or by a raised intra-abdominal pressure, will tend to cause prolapse of the urethral mucosa.

Clinical Findings

The chief complaint in these cases is "spotting" of blood on the patient's garments. This results from trauma of the prolapsed mucosa. This may be accompanied by dysuria, which may be severe when the prolapsed mucosa is strangulated, and even give rise to retention of urine. The prolapse involves the entire circumference of the urethra. The lumen of the urethra is thus completely surrounded by an oedematous and bruised ring of tissue. It is therefore distinguished from the urethral caruncle which involves only a portion of the meatus, usually the posterior lip. A urethral polyp protrudes from the centre of the urethral lumen. A urethrocele produces a swelling through the vagino-urethral septum and is covered by vaginal epithelium. Carcinoma of the urethra may have to be distinguished from the urethral prolapse in the older patient. The carcinoma is indurated and friable, and bleeds easily on examination. In some cases biopsy may be needed to distinguish the one from the other.

Treatment

Since vesical tenesmus may be an aetiological factor in the production of the urethral prolapse it would seem to be a wise precaution to exclude any lesion in the bladder by cystoscopic examination. Further, since the prolapsed mucosa is often inflamed (especially when there is strangulation), it follows that the area should be cleaned with sitz baths to reduce infection to a minimum before any cutting operation is carried out.

Simple digital replacement of the mucosa has been advocated, but the chances of recurrence are great. Berry and Greene (1938) record the case of a patient of 10 years who, one year before being seen, had a swelling of the urethral orifice following a fit of coughing. This had been treated by the patient's mother by rest in bed and local applications with apparently a good result. Recurrence occurred with another fit of coughing, when she was seen and treated surgically.

Livermore (1921) favours four-point fulguration of the mass to induce submucosal fibrosis and so bring about reduction of the prolapse. Hepburn (1927) is more radical in his treatment. Since he maintains that there is a partial hernia of the bladder through poor supporting structures around the bladder neck, he pulls up the bladder through a suprapubic approach and attaches it to the back of the pubic bones and anterior abdominal wall. Keefe (1917) is in favour of replacing the prolapsed mucosa and then, through a vaginal incision, shortening the constrictor muscles around the lower end of the urethra.

The remaining methods of treatment involve removing the prolapsed portion of urethra. A catheter has been placed in the urethra and a ligature tied around it and the prolapsed mucosa. This is left until the prolapsed ring of mucosa sloughs off. The ring of mucosa has been amputated with the electric cautery without any suturing, as suggested by Moffett and Banks (1951), or it may be cleanly amputated with the knife and the cut end of the urethra sutured to the cut edge of the meatus as done in the case described above.

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The Heating Appliances (Fireguards) Act came into force on October 1, 1953. The Act makes it an offence for any person to sell or hire (except in certain specified circumstances) an electric or gas fire or an oil-burning heater which is not fitted with a guard conforming to prescribed safety regulations. There are, however, about 4,500,000 such fires, and a further 12,000,000 open solid-fuel fires, already in use in people's homes, to which the Act does not apply, and a large proportion of these are not equipped with adequate guards. Unless their owners provide guards many preventable accidents will still occur. Cotton fabrics and artificial silks are most often involved in burning accidents, and it may soon prove possible to render these materials less inflammable.

Reviews

CONQUESTS OF MEDICINE

Fifty Years of Medicine. By Lord Horder, G.C.V.O., M.D., F.R.C.P. (Pp. 70. 5s.) London: G. Duckworth and Co., Ltd. 1953.

Goethe in *Kunst und Altherthum* wrote of Sir Walter Scott's *Life of Napoleon*:

"What could be more delightful to me, than leisurely and calmly to sit down and listen to the discourse of such a man, while clearly, truly, and with all the skill of a great artist, he recalls to me the incidents on which through life I have meditated, and the influence of which is still daily in operation."

Those members of our profession who have had the privilege of working with Lord Horder or of being his pupils can re-echo these words of Goethe as they open this slim volume, an expanded version of the Harben Lectures which the author delivered at the Royal Institute of Public Health and Hygiene in December, 1952. The book will be equally appreciated and valued by the younger medical men and women who now enjoy the fruits of the conquests in the realm of scientific medicine which Lord Horder and his contemporaries throughout fifty years have achieved.

Lord Horder, like Tennyson's Ulysses, is not only a part of all that he has met, but is also "honoured by cities of men and manners, climates, councils, governments," and "has drunk delight of battle with his peers." Even those who differed from him could not help but recognize the courage with which he has urged his convictions.

Succinctly, and in good English prose, he indirectly narrates his Odyssey in these pages. The first lecture describes "The Birth of Scientific Medicine," and recalls how the lecturer "took the bench to the bedside"—that is, he introduced clinical pathology to the wards. The second lecture, "Medicine Enlarges its Boundaries," treats of the important advances in knowledge of nutrition and food, physical medicine and rehabilitation, industrial medicine, and nursing. In the third lecture, "The Present and the Future" are briefly surveyed, and certain constructive criticisms are made of the National Health Service.

This is a book to keep and treasure for its wisdom and historical value. *Magna est admiratio copiose sapienterque dicentis.*

ARTHUR S. MACNALTY.

CIVILIAN HEALTH IN WAR

Medical History of the Second World War: Civilian Health and Medical Services. Edited by Sir Arthur Salusbury MacNalty, K.C.B., M.D., F.R.C.P., F.R.C.S. Volume I: The Ministry of Health Services; Other Civilian Health and Medical Services. (Pp. 441. £2 5s.) London: H.M. Stationery Office. 1953.

This is the sixth volume published so far of the Medical History of the Second World War. Sir Arthur MacNalty, who is the editor-in-chief of the complete work, has edited this volume himself. It deals mainly with England and Wales and the Channel Islands. Volume II of "The Civilian Health and Medical Services" will deal with Scotland, Northern Ireland, and the Colonies, and with the medical services of the Ministry of Pensions.

It is only when the material is presented in one book that the far-reaching effect of the impact of war on a well-organized community can be realized. Established services are disrupted; staff disappear; buildings are requisitioned; new problems arise, and new machinery, devised to meet them, must be produced. The book not only describes the state of the various fields of public health activity at the beginning of the war and what happened to them during the war, but also the steps taken at the end to revive them. Full information is given of the action taken to distribute food. "The rationing provision for children and the priority classes went beyond maintaining pre-war diet and aimed at providing an optimum diet." Credit is given to the British Medical Association for its foresight in compiling in 1937 a register of doctors so that, when the blow struck, the selection of those to be recruited could be made with least disturbance to civilian needs.

Air-raid shelter problems and the provision made for the welfare of evacuees, refugees, and the homeless are described in detail. No definite conclusion is reached on why we escaped devastating epidemics, though several suggestions are made. At the beginning of the war cerebrospinal fever became more prevalent; there was an increase in the mortality from tuberculosis and in the incidence of scabies; epidemic jaundice became a problem; but venereal disease was kept in check, and the steps to prevent the spread of malaria, typhus fever, and smallpox were successful. Influenza was feared, but never attained epidemic proportions. There was "considerable reduction in the amount of mental disorder during the first two and a half years of the war." There were 151,936 confinements in emergency maternity homes, with a maternal mortality of 0.8 per 1,000, a stillbirth mortality of 19.3, and a neonatal mortality of 9.6 per 1,000. The general conclusion is: "There was little evidence of a lowering of the standard of health during six years of war, and for this no little credit is due to the skill and devotion of insurance medical practitioners."

War tends to stimulate the development of health services. During this war the Public Health Laboratory Service, mass radiography, and special allowances for the tuberculous were started. The diphtheria immunization scheme was pressed, with highly satisfactory results. Authentic information about venereal disease was, for the first time, published in newspapers, and talks were given in the B.B.C. programmes. The Radio Doctor made his début. The W.V.S. was born.

The invaluable work of the voluntary agencies is described, including that of the American Red Cross Harvard Field Hospital Unit. Mention is made of the Civilian Medical Recruiting Boards, who examined 7,100,409 persons, and the medical work of the Ministries of Health, Education, Labour and National Service, Supply, and War Transport is well described. There is a special chapter on Wales and another on the Channel Islands. The heavy tribulations of the latter are discussed by the medical officers of health of Jersey and Guernsey.

The book is written without any attempt to play on emotion. It is a simple, well-written, and well-documented account of an epic story where everyone did what was expected of him or her, and more.

ALLEN DALEY.

RADIOISOTOPES IN MEDICINE

Radioisotope Techniques: Proceedings of the Isotope Techniques Conference, Oxford, July, 1951, sponsored by the Atomic Energy Research Establishment. Volume I: Medical and Physiological Applications. Ministry of Supply. (Pp. 466; illustrated. £2 10s.) London: H.M. Stationery Office. 1953.

In July, 1951, a conference took place in Oxford on radioisotope techniques as applied to various fields of work. The report of the industrial applications appeared earlier this year, and that of the medical and physiological applications has now been published. This report consists of the full texts of the 70-odd papers that were presented in these sections, together with a note of the discussion on each; and even now, two years after the conference, it is a useful survey of this field of work. This is perhaps explained by the international, yet very informal, nature of the conference, where the preliminary results of a large number of laboratories were fully described and discussed.

The papers are about equally divided between medical diagnostic and therapeutic applications of the radioisotopes, and work on intermediary metabolism and the distribution of materials within the tissues. On these subjects the report is as valuable as the conference was, for it collates work from many different centres, yet with surprisingly little overlap between the various papers on similar subjects. Inevitably, the long interval between the conference and publication of its proceedings robs the book of some of its value, but it remains a most important record of a fertile

conference and a representative "cross-section" of the biological investigations to which radioisotopes are applicable. Even now there are few books on this rather forbidding subject that offer such a mine of important information as does this one. Its editing and preparation by unnamed members of the Harwell staff are as excellent, and must have been as laborious, as their preparations for the conference itself. That is saying a great deal, and it as much deserves our gratitude.

E. ERIC POCHIN.

FOOD HYGIENE

Food Hygiene Handbook. By W. Clunie Harvey, M.D., D.P.H., F.R.San.I., and H. A. Perry, F.R.San.I., M.S.I.A. Foreword by Sir William Savage, M.D. (Pp. 159; 34 illustrations. 15s.) London: Heywood and Co. 1953.

A century of strenuous effort in relation to environmental conditions has eliminated most of the serious dangers to the public health. One of the major defects remaining in this field is faulty food-handling, which is rife in Britain. Hygiene in the manufacture, storage, sale, and serving of food is far too often appallingly poor. The number and severity of food-poisoning outbreaks and the high incidence of the dysenteries are cogent evidence of the existence of conditions apt to be ignored because they are largely hidden. This book deals most effectively with the problems and gives the answers. It is intended as a practical guide for the keepers of shops, restaurants, and hotels and for canteen supervisors and housewives. But general practitioners, medical officers of health, and sanitary inspectors will find here much to interest and stimulate them.

The authors carefully and succinctly summarize the law relating to food hygiene and succeed in making legal reading much less painful than usual. Food-poisoning and the provision and equipment of food premises are subjects adequately considered, and people concerned with individual food trades will find their peculiar difficulties discussed, together with guidance for their solution. The food trade and local authorities have still much to do, but so also has the housewife. The results of care before delivery can easily be undone by carelessness in the home. The authors have laid down clearly and shortly a series of rules which the housewife would be well advised to follow in the interests of her family. There is a valuable section on the infestation of food premises and how to destroy the insects concerned. Many of the excellent illustrations are devoted to these creatures and will help in their identification. At the back of the book there are advertisements of food equipment and materials used in food control. They are relevant to the subject-matter, but I feel that, much as I like this publication, I should have liked it more without them.

This book is commended to everyone concerned directly or remotely with the control of food; and the more widely it is read the greater will be the improvement in food hygiene.

C. METCALFE BROWN.

NEUROSYPHILIS

Clinique et Pathologie de la Neurosyphilis. By Professor J. Alves Garcia. (Pp. 160; 36 figures. No price given.) Paris: Masson et Cie. 1953.

The modern treatment of syphilis has so profoundly transmuted its characteristics that the florid manifestations of the disease are becoming less common and the signs of neurosyphilis less obvious. Nowadays cases seldom correspond to the classical descriptions, and the forms of neurosyphilis, which twenty or thirty years ago were so rich and varied, have been considerably modified by modern therapy. During this transitional period in the history of syphilis the author has had the advantage of observing this metamorphosis as professor of psychiatry and physician to the Hospital for Neurosyphilis at Rio de Janeiro, where extensive clinical material has been at his disposal for some twenty years. His readable monograph on the clinical and pathological aspects of neurosyphilis records the results of his accumulated clinical experiences and histopathological investigations, which he hopes will stimulate further research into the newer pathological concepts.

Without being exhaustive or so statistical as to be monotonous, the earlier chapters are complete essays on the various clinical types of neurosyphilis and their pathology. Later chapters are on the pathology and histopathology of parenchymatous syphilis, some original researches on malarial therapy and the irreversibility of its vascular lesions, optic atrophy, congenital neurosyphilis, and a final chapter on treatment.

The many divergencies of opinion on the possibility of dualistic strains of *Treponema pallidum* are fully discussed. The supporters quote the rarity of cerebral syphilis among the American negroes, the Chinese, the Persians, and the natives of Central Africa. But other provocative factors must be recognized such as fatigue, intellectual strain, and alcoholism. Possibly when the virus is not sterilized by energetic treatment it acquires new characteristics and becomes neurotropic. Moreover, modern treatment may have provoked biological alterations in the spirochaete to render it neurotropic rather than dermotropic. Meanwhile, modern research seems to have discarded the thesis of a neurotropic strain of spirochaete.

The author says that malaria therapy for G.P.I. has not been surpassed by any other method of treatment, and penicillin has not had the success which might have been expected. He considers penicillin insufficient treatment for the pure forms of parenchymatous syphilis and would administer it only as an adjuvant in those cases showing intense cellular reaction in the cerebrospinal fluid. He is an advocate of malaria therapy, preferably with malignant tertian in Brazil, for both tabes and G.P.I., and follows it immediately with arsenic and liposoluble bismuth. But he would absolutely forbid the use of all quinquevalent arsenicals in the presence of optic atrophy. These are strong words, coming as they do from a hospital where, during the ten years 1942–52, most of the admissions (62%) were cases of G.P.I.

The author stimulatingly declares that there are no mental symptoms which are specific of syphilis, not even in G.P.I., and provokingly asks why this same condition provides such a variety of symptoms when the anatomical lesions are so invariably the same. And, since they are so uniform, why are the clinical symptoms not equally so? Again, although G.P.I. is generally considered to be non-infectious, he remarks that the blood from such a patient can cause typical granulomatous lesions when inoculated into a laboratory animal. Such numerous incidental observations scattered throughout the book make it well worth reading, for they are the plums from a unique experience and the personal hallmarks of a master of his subject.

T. ANWYL-DAVIES.

A *Catalogue of Engraved Portraits in the Royal College of Physicians of London*, by A. H. Driver, has been published by the College, price £2. In the preface reference is made to previous work by the late Dr. Arnold Chaplin. He devoted many years to the task of building up and describing the collection, and his catalogue forms the basis of the work now published. The biographical data included in the present catalogue show evidence of considerable knowledge of medical history and bibliography, and it would have been more accurate to concede its authorship to Dr. Chaplin and its revision to Mr. Driver. The College now possesses some 4,500 prints, including the large collection given by Chaplin in 1934, and this printed catalogue marks an important step forward in the documentation of such material. Besides dates and brief biographical notes of the subjects, information given on each portrait includes size, painter, and engraver. There is also an alphabetical list of engravers. We must now look forward to the time when catalogues of the comparable collections at the Royal College of Surgeons and the Royal Society of Medicine and the much larger collection in the Wellcome Historical Medical Museum can be published. Equally valuable would be a printed version of the magnificent catalogue of all known engraved portraits of British medical men, compiled some years ago by Chaplin, Herbert Bruen, and W. J. Bishop, which at present exists only in typescript copies at the Royal College of Physicians, the Royal College of Surgeons, the Royal Society of Medicine, and the Print Room at the British Museum.

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RESPONSIBILITY FOR MURDER

The most far-reaching of the conclusions suggested by the Royal Commission on Capital Punishment[1] will probably prove to be those on the M'Naghten Rules, for of the Commission's leading recommendations, summarized at page 775 of the *Journal*, these are the most likely to be accepted in something like their present form. They are largely in accord with the medical evidence presented by the B.M.A. and by the Institute of Psycho-analysis, as well as with that of some, though by no means all, individual medical men who gave evidence. They will have, too, some legal support, and public opinion is unlikely to cavil at them.

In brief, the Commission (with some dissentients) concludes that the Rules should be either amended or abrogated. If amended, they should be enlarged with some such phrase as that suggested by the B.M.A.,[2] so that there would be added to them the test whether the accused was labouring, as a result of disease of the mind, under "a disorder of emotion such that, while appreciating the nature and quality of the act, and that it was wrong, he did not possess sufficient power to prevent himself from committing it." If the Rules are to be abrogated—and the Commission would prefer that—then the jury would have no formula put before it, but would determine, in view of all the evidence, whether at the time of the act the accused was suffering from disease of the mind to such a degree that he ought not to be held responsible. In either case mental deficiency no less than disease of the mind is held to be a possible cause of irresponsibility.

The chief reason why the Commission would have the M'Naghten Rules altered is because they take into account only the cognitive faculties, which is the main criticism the medical profession has made of them—and began making almost as soon as they were formulated over 100 years ago. But the phrase "irresistible impulse" which was so often on the lips of reformers is open to objections also. In the first place, its critics would ask, how is an irresistible impulse to be distinguished from one that is unresisted? An objection perhaps more telling to the medical mind is that it gives a false picture of the mentality of some people arraigned before the courts. Often it was not some overwhelming wave of passion, with an implication of transience, that guided a criminal's conduct so much as a long-continued mental state. Commonly such a condition could be classified as paranoia. This and other mental disorders are often enough accompanied by sufficient clarity of intellect to enable the accused person to know the nature and quality of his act and that it was legally wrong, yet it may be questioned whether any accused thus afflicted has been hanged in recent years. Some have been reprieved by the Home Secretary after a medical investigation, while others have been found "Guilty but insane" under the M'Naghten Rules. This has been possible only because of the considerable latitude with which they have been interpreted. As that great lawyer, Viscount Simon, expressed it in an address published in the *Journal* recently[3]: "Judges and juries are impressed by really strong medical evidence of irresponsibility, and the legal formula is not of cast-iron, but allows of elastic application." It is this elasticity of interpretation that has been invoked both by those who would retain the Rules and by those who would replace them; for, argue the first, rules of some kind are necessary, and a humane application of them has made them work in practice; while the second contend that rules with which such liberties have to be taken to conform to public opinion of the day are better scrapped altogether. The Commission has taken the second view, and there is much to be said for it. Whether it would prove workable in practice is another matter. An extension of the Rules may be preferred, and in that case medical opinion would seem to be well met by the Commission's suggestion of adding to the formula a phrase to the effect that the accused, as a result of disease of the mind (or mental deficiency), "was incapable of preventing himself from committing" the act.

But whatever of the suggested modifications is made to the M'Naghten Rules the formula is bound, so long as it is retained, to have the defect of any formula applied to the infinite variety of human experience. In attempting to distinguish between the responsible and the irresponsible, judges and juries are likely to be harassed by those puzzling cases in the borderland where reason glows dimly but is not extinct. With this in mind the B.M.A. included in its evidence a recommendation that a verdict of "guilty with diminished responsibility" should be returnable in suitable cases in the English courts as it is in the Scottish. The Commission was unable to agree. Its main objection is against trying to take a doctrine that has grown up gradually in the common law of Scotland and inject it in one dose into

[1] *Report of Royal Commission on Capital Punishment*, 1949–53. 1953. H.M.S.O. 12s. 6d.
[2] *British Medical Journal*, 1950, 1, 365.
[3] Ibid., 1953, 2, 1.

the English law; but, recognizing that some alteration in the present state of things may be necessary, the Commission embarks on the highly controversial argument that the jury should have the power of deciding whether the prisoner should hang or whether mitigating circumstances demand a lesser sentence. We pass here beyond the borders of medicine into those many other problems that the Commission sets before us on which a doctor's opinion will owe less to his medical training than to his private judgment.

Among the recommendations of special interest to medical men is one that has achieved some considerable publicity—namely, that on execution by injection of a lethal drug. While the Committee does not recommend lethal injection "in present circumstances," it does recommend, "unanimously and emphatically," that it should be considered periodically. Here most medical men will feel that the Commission has gone rather astray. Whatever may be said for or against various procedures for causing death speedily and humanely, the Commission does not touch on what to practising doctors must be one of the strongest arguments against lethal injections. It is that the injection of a drug is a procedure that was invented and has always been used wholly for beneficial purposes, and it is so regarded in the public mind. To execute criminals by the same procedure as brings ease and sleep to sufferers from pain must surely arouse, even if unconsciously, feelings of abhorrence in many people. No emphasis is needed to the evidence put before the Commission by the B.M.A. that no medical man would be associated with the giving of lethal injections or the training of other people to give them.

ANTIBIOTICS IN WHOOPING-COUGH

The unusually high number of whooping-cough cases being reported in England and Wales each week is illustrated graphically in our epidemiological columns. It remains a serious disease, especially in very young children, and unfortunately antibiotics offer no dramatic benefits. *Haemophilus pertussis* is highly susceptible *in vitro* to the action of the newer antibiotics, yet their efficacy in the treatment of the disease is still uncertain. This is perhaps not surprising in view of the fact that, in the untreated disease, *H. pertussis* disappears early from the clinical picture, though symptoms persist and often increase for several weeks after it can no longer be detected. Perhaps *H. pertussis* induces an altered state of the tissues which is responsible for the symptoms, and once this state is induced the presence or absence of the organism is of little account. A drug whose only action is to inhibit *H. pertussis* could not be expected to alter the course of the disease unless it were applied before the tissue reaction had been induced. While this is no more than conjecture, something of the sort may explain the discrepancy between clinical and laboratory results.

A report[1] published by the Whooping-Cough Subcommittee of the Antibiotics Clinical Trials Committee of the Medical Research Council analysed the results of treatment with chloramphenicol, aureomycin, and an inert control preparation in 294 patients. Children aged 0–11 months were given 1 g. daily in two doses, children aged 12–35 months 1.5 g. daily, and children aged 36–59 months 2 g. daily, in each case for seven days. The effect of the treatment was judged by the frequency and severity of the spasms and by the culturing of per-nasal swabs. The bacteriological evidence was clear: treated cases cleared more rapidly than controls. Clinical effects were much less striking, and it was mainly in cases treated within eight days of the onset of the earliest symptoms that any significant difference was found. The report emphasizes that these earliest symptoms are cough or coryza, not the development of a paroxysmal cough, which for this purpose must be regarded as appearing at a relatively late stage of the disease. It is also clear from the report that even in the early group results of treatment were not dramatic: indeed, most of the children were still having typical spasms three weeks after the start of treatment. The drugs appeared to diminish the severity of the paroxysms to a greater degree than their number. But in cases treated later than eight days after the onset of symptoms the difference in number and severity of paroxysms between treated and control groups was very slight, though always in favour of the treated group. As the report states, if attention had been directed to a comparison between the whole of the treated and of the control groups, it would have been concluded that chemotherapy failed to produce a clear-cut clinical cure.

Gray,[2] commenting on the report, criticized a dosage scheme based on age rather than tissue mass. He worked out the equivalent doses per kg. body weight: these range from 50 mg. to 75 mg. per kg. It is quite possible that such doses are not high enough, but they are not unreasonably low. Gray then quoted some figures of chloramphenicol concentrations in post-mortem lung and brain tissues showing that concentrations of the drug vary from tissue to tissue, that vascular obstruction coincides with low concentration, and that in uninflamed human

1 *Lancet*, 1953, **1**, 1109.
2 Gray, J. D., ibid., 1953, **1**, 1257.
3 —— ibid., 1950, **2**, 800.
4 LaBoccetta, A. C., and Dawson, K. E., *Amer. J. Dis. Child.*, 1952, **84**, 184.
5 Lassen, H. C. A., and Grandjean, L. C., *Lancet*, 1951, **1**, 763.
6 Hazen, L. N., *et al.*, *J. Pediat.*, 1951, **39**, 1.
7 Booher, C. E., *et al.*, ibid., 1951, **38**, 411.
8 Bogdan, A., *Lancet*, 1951, **1**, 764.
9 *British Medical Journal*, 1952, **2**, 136.

lung chloramphenicol is rapidly removed. These are points of considerable importance, suggesting that different dosage may be required at different stages of the disease, but whether they can be translated into a practical dosage scheme is another matter. In an earlier paper Gray[3] investigated the use of aureomycin and chloramphenicol in the treatment of whooping-cough: for aureomycin the dosage was 50 mg. per kg. per day in four doses, for chloramphenicol 100 mg. per kg. per day in one dose, in both cases for a total of five days. He found that both drugs reduced the number of coughs, but that chloramphenicol also lessened the whooping and vomiting and loosened the cough. His results showed no dramatic change in the course of the disease: children were still having paroxysms three weeks after the onset of the disease, but the number of paroxysms was less than in the controls. He suggested a higher dosage scheme.

Other workers have had similar experiences. La-Boccetta,[4] using aureomycin in a dosage of 50 mg. per kg. body weight for ten days, concluded that, except in cases treated in the first week of the disease, there was no marked apparent effect from the use of the drug. Lassen[5] treated 93 cases with chloramphenicol, given as rectal suppositories for three to five days, and claimed that the frequency of the paroxysms fell sharply. No untreated controls are reported for comparison, and patients were still having paroxysms at the end of the period of observation, though fewer in number. Hazen[6] and Booher[7] used terramycin as well as the other two drugs, and it appears to have a similar degree of efficacy. Bogdan[8] used chloramphenicol to treat contacts, and his results are striking: in 10 out of 13 cases the disease was arrested in the pre-paroxysmal stage. The treated contacts must be isolated from infectious cases to avoid reinfection.

It is clear that no drug has yet been discovered which will rapidly control an attack of whooping-cough. Aureomycin, chloramphenicol, and terramycin probably all have some effect if given in the earliest stages, but the effect is far from dramatic. When given later in the disease they have very little effect. These drugs have toxic effects—most notably chloramphenicol[9]—and it is inadvisable to prescribe them in every case. The minimal dosage is 50 mg. per kg. body weight per day, and 75 or 100 mg. per kg. may be better given in three or four doses per 24 hours for seven days. Because babies under 1 year suffer most severely from the disease, it is justifiable to treat all patients of that age. All cases diagnosed within a week of the first symptom—not the first spasm—might also be treated. Even in these cases dramatic results should not be expected. Probably the most rational use of the drugs is in the treatment of contacts before they develop the typical symptoms of the disease.

SEVERE REACTIONS TO PENICILLIN

It has long been recognized that sensitivity to penicillin may develop, certainly in consequence of treatment and possibly in other ways. Some of the penicillin in the blood is bound to plasma proteins, and it therefore evidently behaves as a haptene. As long ago as 1945 A. Rostenberg and H. Welch[1] found 5% of subjects to be sensitive as determined by intradermal tests. S. M. Peck and his colleagues[2] found this condition in 5.4% of 499 subjects, and in a higher proportion of those who had been treated with penicillin. These authors and R. Schuppli,[3] who observed a marked increase in the frequency of sensitivity between 1947 and 1951, also consider that skin mycoses predispose to it; whether antigenic relationships or simply an allergic diathesis are responsible for this seems uncertain. The usual effects of giving penicillin to such a patient in these earlier times were fever and urticaria.

More recently much more alarming and even fatal reactions have been described. Following the paper by F. J. Pick and J. F. Patterson[4] recently published in this *Journal* describing a fatal reaction to a penicillin injection, and the report in our medico-legal columns[5] of an inquest on a similar case, we have had several letters, some which appear in our correspondence columns this week, describing similarly alarming but fortunately non-fatal reactions. Experiences of this kind, although apparently new, are by no means unique: Bayer and five colleagues,[6] writing from Illinois, describe six such occurrences, one being fatal, and are puzzled that so little has been written on this subject "in view of the ease with which this series was collected in a short period." Since there appears to have been nothing unusual in their methods of giving the drug, such reactions cannot be very uncommon, and it is important to know how to prevent them.

In the first place, suction before injection should always be practised in order to ensure that what is intended to be an intramuscular injection is not in fact intravenous. The subcutaneous route is perhaps preferable on this account, since the likelihood of entering a vein is then remote. Intravenous sodium penicillin is harmless in a normal subject, but penicillin in some of its present forms is not. If the preparation contains oil, or procaine penicillin crystals in suspension, these are at least liable to obstruct lung capillaries, while some of the more complex penicillin compounds, including that used by Pick and Patterson, are suspected of exerting an actually toxic effect when accidentally injected intravenously.

This is certainly not the explanation of every such reaction, since one in the series of Bayer and his colleagues resulted from nothing more than the intradermal injection of 10 units of crystalline penicillin as a test of sensitivity. The other factor is unquestionably sensitization: such patients always give a history of previous penicillin treatment, and often of previous reactions of some kind. The fact that they have been sensitized can

1 *Amer. J. med. Sci.*, 1945, **210**, 158.
2 *J. Amer. med. Ass.*, 1948, **138**, 63.
3 *Schweiz. med. Wschr.*, 1951, **81**, 589.
4 *British Medical Journal*, 1953, **2**, 605.
5 Ibid., 1953, **2**, 446.
6 *J. Amer. med. Ass.*, 1953, **151**, 351.
7 *Arch. Derm. Syph. (Chicago)*, 1950, **62**, 314.

be proved by the intradermal injection of a small dose, the usual result of which is immediate wheal formation. The time has apparently come when at least some cursory inquiry about previous reactions should be made before giving any patient penicillin: a test for sensitivity should follow if the history is suspicious. Patients having asthma or other allergic conditions should evidently be treated with caution. The administration of an antihistamine compound with the penicillin itself, according to S. W. Simon and M. D. Feldman,[7] serves to prevent the ordinary type of hypersensitivity reaction, and would presumably have a similar effect on the more severe. Drugs of this type are also apparently at least as useful as adrenaline for the treatment of the established reaction.

It would be most unfortunate if, as one of our correspondents seems to suggest, this development tempts doctors to abandon penicillin for one of the newer antibiotics. Penicillin has properties possessed by no other drug, and what is chiefly required is greater discrimination in its use.

CULTIVATION OF THE COMMON COLD VIRUS

At the end of the last war the Harvard Hospital at Salisbury, originally designed and shipped to the United Kingdom for the study of infectious disease arising in the European theatre of operations, was most generously handed over by Harvard University to the British Government for the study of problems in preventive medicine. For the last seven years it has been the centre of research into that most common of all human afflictions, the common cold. The starting line for this enterprising project was acceptance of the belief that the primary aetiological agent of the common cold was a virus. Dochez[1] had shown this to be so more than twenty years ago, and it has since been confirmed on numerous occasions by Andrewes and his colleagues at Salisbury.[2] Having accepted this fact, research workers had as their first and main objective to catch the virus and study it under laboratory conditions. It may seem strange that a virus which is capable of causing such universal and indiscriminate disease in man should be so difficult to adapt to laboratory life. But so it has been. Despite innumerable attempts, aided by all the tricks of the trade, the common cold virus has, with the exception of Dochez's success with chimpanzees, resisted all the efforts made to cultivate it outside the human host.[3] How then could this objective be reached? The successful adaptation of poliomyelitis viruses to tissue culture of human embryonic material pointed to a new line of attack on other viruses pathogenic to man.[4]

Earlier experiments with the common cold suggested that the virus at least survived in human embryonic tissues. Now with improved technique Andrewes and his team present evidence that actual virus multiplication has taken place.[5] Using the roller-tube technique with explants of human embryonic lung and a single strain of virus, they have brought on colds in human volunteers by intranasal inoculation with material up to and including the tenth serial passage. Some intermediate passages have been negative, but colds artificially induced do not always "take." Controls, however, have been clearly negative. The repeated dilution that has necessarily taken place on passage suggests that the colds produced at the tenth passage have been caused by fresh virus rather than by any virus remaining from the original inoculum.

Human volunteers have so far played an indispensable part in this work as indicators of the presence of virus in test material. The second objective will therefore be to find some method of identifying the presence of virus without recourse to human beings. Cytopathogenic effects, a noticeable feature in poliomyelitis tissue cultures, have so far not been observed in the case of the common cold. More detailed microscopical examination and immunological tests may provide a way of overcoming this obstacle. It seems clear that further calls will be made for human embryonic material in modern virology. For understandable reasons, supplies of such material in this country will fall short of demand, and so it is important that the fullest possible use is made of any material that is available until such time as a more convenient medium can be found.

1 *J. exp. Med.*, 1930, **52**, 701.
2 *Lancet*, 1949, **1**, 71.
3 Andrewes, C. H., *New Engl. J. Med.*, 1950, **242**, 235.
4 *British Medical Journal*, 1953, **1**, 826.
5 *Lancet*, 1953, **2**, 546.

OCCUPATIONAL FERTILITY

The last part of the Registrar-General's 1931 Decennial Supplement[1] has just appeared; it is mainly on occupational fertility. The crude birth rate per 1,000 married males aged under 55 in 1931 was, for all classes combined, 95.9. The crude birth rates of social classes I to V expressed as percentages of that for all classes were, respectively, 75.1, 67.6, 99.4, 110.4, and 127.4. There were fluctuations within the social classes, and the most remarkable for occupational groups with 1,000 married men or more was that of company directors (so returned) in finance and insurance in social class I, who had a ratio of 277.9. This ratio was much the largest recorded. After that the other ranks of the Services had the highest birth rates, the percentage ratios of their birth rates to the rate for all classes being 228.2 for the Royal Air Force, 213.7 for the Army, and 194.9 for the Royal Navy and Marines. The ratios for the Merchant Navy were much the same, being 204.5 for petty officers, seamen, and deck hands, 203.6 for pursers, stewards, and domestic staff, and 202.6 for firemen, trimmers, greasers, and donkeymen. The largest ratios among civilian occupations were greengrocery salesmen and shop assistants 190.6, other assistants to furnacemen and rollers 190.0, builders' labourers 184.7, haulage and cartage contractors, managers, and master carmen 174.2, slaters and tilers 166.5, tube drawers and welders 161.4, motor mechanics (so returned) 159.0, constructional engineers (not professional) 152.0, other dock workers 149.5, miners, other workers below ground 148.6, miners, hewers, and getters 147.2. The lowest ratios were those of metal workers, foremen, and overlookers in machine shops 12.7, and heads or managers of commercial

1 *Registrar General's Decennial Supplement, England and Wales. 1931.* Part IIB, Occupational Fertility, 1931 and 1939.

offices 17.0. Generally the group of foremen and overlookers had a very low ratio, and in nineteen types of occupations with 1,000 or more married men aged under 55 the ratios varied between 20 and 40. Other very low ratios were lodging- and boarding-house keepers 19.8 and chief constables, inspectors, and superintendents of police 22.1.

Most of these differences are not so much occupational as due to age, for a parent has commonly founded and perhaps reared his family before attaining a position of responsibility. The difference between the younger and older men can be readily demonstrated with railway workers. In the period round 1931 the locomotive engine fireman had to serve several years before promotion to engine driver, and during his spell of firing he married and started a family. In 1931 the ratio of the crude birth rate to that of all occupations was 143.9 for firemen and only 44.2 for engine drivers.

A comparison has been made between the relative fertilities of married men aged under 55 and their wives aged under 45. The index for each sex was found by expressing the birth rate for each population group as a percentage of the rate for all classes combined. The index for each sex was in very close agreement, and generally differences of 5 or less were recorded. But fishermen were an exception, for the married men had a birth rate in 1931 of 79.0% of all males, while the married women had a rate of 139.7% of all married women.

Some data for 1939 included in this volume were analysed by thirteen occupational groups. The wives of miners had the lowest average age at marriage of 23.3 years, the lowest at first maternity of 25.1 years, and the shortest average duration between marriage and first maternity of 1.8 years. On the average the wives of professional and administrative workers married at 25.9 years, and had their first child at age 28.6 after a marriage duration of 2.7 years. The wives of miners had the highest stillbirth rate, while the professional classes had the lowest.

Twenty-two and a half years have passed between the 1931 Census and the publication of this volume, though the inclusion of information collected in 1939 is some compensation. Doctors and others who are interested in such information as the Registrar-General publishes here would be better served if it concerned contemporary rather than historical events, and many will hope that the results of the 1951 Census will not be so delayed.

PREVENTION OF FOOT DEFECTS

In an ageing population there is bound to be a steady rise in the incidence of disabilities due primarily to wear and tear. This applies especially to foot defects, which have become a serious medical problem. It is economically impracticable, even if it were possible, to provide effective treatment for all those with established foot defects, and under the National Health Service it has been considered an economic impossibility to provide chiropodial treatment for all, because the demand would be so great. A close analogy may be drawn between the foot and the motor-car. Although cars of varying quality are produced, they are all capable of giving good service provided that they receive careful maintenance. The need for specially equipped repair shops is in inverse proportion to the care with which cars are serviced. The same applies to the human foot, but so far we have concentrated on providing expensive specialist services and elaborate equipment for the repair of broken-down feet, when what is required is an organization for their care and maintenance, especially during the running-in period—that is to say, during childhood. One factor that has delayed the development of such services is the lack of factual information about the incidence, aetiology, and mode of development of the various types of foot defects. As a result of recent surveys, however, the general picture is becoming much clearer. The information afforded by the survey[1] conducted in the borough of Luton on the incidence of foot ailments at all ages among the general population has now been reinforced by two further surveys whose results are published in this issue of the *Journal* (pp. 745 and 749). The conclusions that may be drawn from these and other investigations should be of assistance in the planning of preventive measures.

Perhaps the most important point brought out by all investigations is the fact that the majority of those defects which are responsible for the more serious disabilities of later life are already well established by late adolescence. A second fact of almost equal significance is that, although a foot may have a congenital weakness rendering it liable to develop some particular defect, whether it does so or not depends primarily upon the care it receives during childhood and adolescence, with special emphasis on footwear. An obstacle to the comprehensive organization of preventive measures lies in the multiplicity of the various interests involved, from the public health and school authorities on the one hand —with their teams of workers comprising doctors, health visitors, school nurses, physiotherapists, and chiropodists —to the shoe manufacturers and retailers on the other. Finally, there is the fact that the foot is a complicated piece of mechanism demanding knowledge and understanding for its proper care. Before real progress can be made much closer co-operation is needed between the diverse interests concerned, and a better and more general understanding of the problems. The Boot and Shoe and Allied Trades Research Association and the Foot Health Educational Bureau have already done much good work on these lines. Now that the latter has been taken under the wing of the Central Council for Health Education it is to be hoped that it will have the opportunity for increasing the scope of its work still further. The fruits of co-operation are already evident in the plans for a "foot health week" to be held in Birmingham later this month under the aegis of the Foot Health Educational Bureau and the Birmingham health and education departments.

Further knowledge could now best be gained by conducting pilot experiments in foot care in various parts of the country. A provisional pattern for such experiments has already been worked out, the essential features comprising the regular inspection of the feet of school-

[1] Dykes, R. M., Grundy, F., and Lee, H. E., *Med. Offr*, 1952, **87**, 223 and 235.

children, the assessment of the significance of any defects noticed by those with the requisite training and experience, advice and regular supervision in the matter of footwear, and arrangements for special treatment in selected cases. Fortunately, for once, the requirements do not entail great expense on elaborate equipment, buildings, or staff. Although local health and education authorities already have their hands full with other urgent tasks, it is very much to be hoped that more of them will take the initiative in helping with this important aspect of preventive medicine.

QUALITY IN GENERAL PRACTICE

It might be thought that a good postgraduate grounding in clinical medicine would be apt to make a man pre-eminently suited to general practice. But the difficulties experienced by many holders of higher qualifications, and especially the M.R.C.P., in entering general practice suggest that there are at least some established doctors who do not share this view. Another aspect of this problem was discussed in the General Medical Services Committee of the B.M.A. last year,[1] when Mr. R. M. Forrester, chairman of the Registrars Group Council, put before the committee the anxieties and needs of registrars for whom no consultant openings would be made. He received the sympathetic hearing that his case deserved. But while the problem was rather a different one with its own special urgency then, its discussion served to throw light on the more general question whether postgraduate study is in fact the asset it is sometimes claimed on paper to be when a doctor seeks an entry into general practice. Several speakers expressed the view—and no one can cavil at it—that a doctor, however well qualified in medicine, must begin at the beginning when he starts in general practice, and not expect to become immediately a principal in a large practice ready-made for him. Nor, indeed, is he likely to get far if he enters general practice with an air of doing so as a last resort and with an expectation of obtaining part-time hospital work straight away. Those responsible for his appointment to a vacancy, whether as assistant or principal, may well take care to assure themselves that he intends to devote his whole energy to general practice. But when allowance is made for those few registrars who take no heed of such criteria as these, there remain many who believe that they have been turned down for no other reason than that they have done several years of postgraduate medical work in hospital and achieved a higher qualification. In a letter at page 161 of the *Supplement* this week a correspondent draws attention to the plight of some of these people. Whatever may be said for or against his specific cases, there is more than a grain of truth in the jocular remark—which came from a good source—that to the applicant for a general-practice vacancy the possession of a car is more important than the possession of an M.R.C.O.G., F.R.C.S., or—most dangerous encumbrance—M.R.C.P.

While there is an obvious truth in the assertion—and it has needed emphasis recently—that general practice is a special branch of medicine, there is the danger too that the hypnotic reiteration of a catch-phrase may obscure the fact that the greater part of general practice is still clinical medicine. It may gather tributaries from other springs of knowledge, but surely a thorough foundation in ordinary general medicine to the M.R.C.P. standard can be nothing but an asset. And so it is held to be for even the much more restricted medical specialties, such as, for instance, anaesthesia or dermatology, many of whose consultants have a higher postgraduate qualification in general medicine. There are already far too many barriers to free and easy movement in the Health Service. Most of them are inherent in its administrative structure, and doctors have rightly condemned them many times. It would be deplorable if a few but influential people in our own profession should heap up more barriers, and ones peculiarly harmful to that lively spirit now to be seen animating general practice in many quarters.

[1] *British Medical Journal Supplement*, July 26, 1952, p. 77.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

One of the facilities general practitioners have been seeking for some time is easier access to pathological investigations, though one may note as a corrective to this that in the G.P. Review Committee's report[1] some 50% of general practitioners did not think their practices suffered from the absence of such facilities. Nevertheless it is difficult to see how general practitioners can do what one witness in the inquiry[1] described as "good medicine" unless he has at his disposal the exact information and guidance a clinical pathologist can give him. General practitioners will want to know just what facilities are available, how they may make use of them, and how they may interpret the findings of the laboratory so as to use them for the benefit of their patients. It is for this reason that we are publishing over the next few months a series of articles on "Clinical Pathology in General Practice," the first of which, by Professor S. P. Bedson on "Facilities under the National Health Service," appears at page 774. Future articles will be on such subjects as the method of collecting specimens, technique of venepuncture and lumbar puncture, taking specimens for medico-legal purposes, and on the value of various tests and investigations in the diagnosis of disease. Throughout it is hoped to give the normal values of various bodily constituents so that the practitioner may constantly have these by him; and the writers in this series will discuss the significance to be attached to variations from the normal. As Professor Bedson puts it: "The important thing is that the general practitioner should consult with the pathologist about his case, for only in that way will he get full value from this service." Such a consultation should be of the highest interest to both, for it will bring the pathologist into more direct contact with the everyday problems of practical medicine and give the practitioner a more exact idea of the help the science can give the art. And the patient will benefit. It is hoped that the present series will make such co-operation fruitful.

[1] *British Medical Journal*, September 26, 1953.

CLINICAL PATHOLOGY IN GENERAL PRACTICE

FACILITIES UNDER THE NATIONAL HEALTH SERVICE

BY

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This century has seen enormous progress in the application of pathology to the elucidation of clinical problems. Fifty years ago the pursuit of pathology was largely academic. It was, of course, recognized as being fundamental to the science of medicine, and morbid anatomy and histology were used to a limited extent for the purpose of solving clinical problems in retrospect. But a diagnostic service of hospital pathology such as we have to-day, in which microbiology, biochemistry, and haematology take their place with the more ancient discipline of histopathology, had hardly been conceived. By the outbreak of the second world war the teaching hospitals and the larger voluntary hospitals had built up departments of pathology which not only provided a diagnostic service but served also in many instances, and particularly in the case of the teaching hospitals, as active centres of research. But this was not the case in many municipal or small voluntary hospitals which at that time either lacked completely, or were ill supplied with, such an essential aid in the treatment of their patients. And nothing had been done to supply the wants of the general practitioner in this respect, if one excludes one or two commercial or local authority ventures which in the main provided a limited postal pathology service of a most undesirable kind.

The consequences of war are not invariably evil, and one of the good things achieved by the recent war was the raising of the standard of medicine in the more isolated and less advanced hospitals of this country. This was the outcome of the Emergency Medical Service with its transfer of staff, equipment, and ideas from the efficient hospitals of our large cities to the more lowly and sometimes rather primitive institutions in the less congested parts of the country. Upgrading these hospitals was not merely a question of implanting in them a leaven of good clinicians; all the other services had to be installed or improved, and that meant setting up adequate departments of pathology, because, as all are agreed, a good service in pathology is essential to a high standard of achievement in medicine. And when in 1948 the National Health Service came into being it was very largely on the pattern evolved during the war that the service was fashioned, at any rate so far as pathology was concerned. There was, however, this difference, and a very important one at that: the pathology service envisaged by the designers of the health service was to be just as readily available to general practitioners as to the clinical staff of the hospitals.

One ought, perhaps, to say that the general practitioners did at times make use of the Emergency Laboratory Service, and in this they were not discouraged either by the local authorities or by the Ministry—in fact, in some parts of the country the service was thrown open to them. For example, the county laboratory service with which I was associated in the war was made freely available to the practitioners, and very popular it proved. But this is a different matter from the nation-wide service in pathology which, in theory at any rate, became available to the general practitioner with the passing of the National Health Service Act. There can be no two opinions about the value of such a consultant service to those engaged in general practice, but it should be clearly understood that what one has in mind in saying this *is* a consultant service and not just the provision of laboratory aids for general practitioners.

Scope of the Service

One knows, of course, that general practice can be carried on without any help from the laboratory at all, and Duncan (1952), who practises in Portsmouth and who, incidentally, is an enthusiastic advocate of a general-practitioner service in pathology, reckons that about three-quarters of his patients can be satisfactorily treated without recourse to laboratory aid. There is little help, for instance, which the laboratory can give in the diagnosis of the exanthemata, with the exception of smallpox, of mumps, or of the common cold, and, as Duncan rightly says, there is no need to seek the aid of the pathologist in connexion with the diagnosis of influenza when this condition is epidemic. The sporadic case would, however, present an entirely different problem, for without the context of similar cases it might be difficult to distinguish it from pyrexias of undetermined origin, and in the investigation of such febrile states the help of the laboratory can be invaluable. And there are many other conditions in the diagnosis and the treatment of which the general practitioner will find consultation with the pathologist and the resources of the laboratory an advantage and sometimes a necessity: urinary tract infections, disturbances of renal function, renal failure, the many forms of anaemia, hepatitis, the virus pneumonias, and the control of the therapeutic use of such preparations as liver, vitamin B_{12}, thiouracil, and the antibiotics are some of these.

In addition to these investigations of a more or less routine type there are certain special ones which should be mentioned. Selective weed-killers of the dinitro-*ortho*-cresol (D.N.O.C.) type are much used these days for the various corn crops. They are applied to the growing crops in the late spring, and, although they are highly toxic for man, their continued use is widespread because of the greatly increased yield per acre which they make possible. The wearing of masks and protective clothing reduces the risk of poisoning to negligible proportions, but cases of poisoning have occurred and knowledge of the level of D.N.O.C. in the blood is helpful diagnostically, and also as a warning of impending intoxication. Hospital laboratories situated in strategic positions throughout the country undertake this investigation.

Another agricultural hazard comes from the use of organic phosphorus insecticides, such as diethyl-*para*-nitrophenyl-thiophosphate ("parathion"), by the fruit growers. Poisoning by these preparations results in destruction of cholinesterase, and the estimation of the blood level of this enzyme is useful to the doctor both in the diagnosis of parathion poisoning and in its prevention. Four laboratories undertake this particular investigation; they are

situated in Worcester, Peterborough, South-east London, and Portsmouth, near to the important fruit-growing districts where these particular insecticides are most used.

A third special investigation concerns the diagnosis of pregnancy. There are several tests available for this purpose, and of these the Hogben test, which makes use of the *Xenopus* toad, is probably the most satisfactory. Not infrequently it is necessary for *medical* reasons to know at the earliest possible time whether or not a woman is pregnant, and pregnancy-test centres have been established, at Watford and at Sheffield, to investigate these cases.

A Consultant Service

The description of the pathological service available to the general practitioner has been made in very general terms; specific mention of what to send, and when or how and to whom, has been avoided. This has been done deliberately. For one thing this article is to be followed by others dealing in a more detailed way with particular aspects of the general-practitioner laboratory service, and the answers to some of these questions will be found in them. But it has been done for a much more important and fundamental reason: to emphasize that this service in pathology offered by the National Health Service to the general practitioner is a consultant service and not a penny-in-the-slot business; for that would be no better than the postal services of the past. If a general practitioner wishes to make use of the service he should get in touch with the nearest pathologist and tell him what his problem is. It may be that it will suffice to send a specimen to the laboratory, or possibly it may require sending the patient, in which case an appointment can be made. If the patient cannot be moved it may necessitate a domiciliary visit, or, of course, it may be one of those cases in which the pathologist cannot be of help. The important thing is that the general practitioner should consult with the pathologist about his case, for only in that way will he get full value from this service.

There is another aspect to this. The general-practitioner service and the hospital service are both parts of the National Health Service equal in importance with the third component, the public health service, and, as Sir Allen Daley (1953) has pointed out in his Croonian Lectures, these three parts of the Service will make a more effective contribution to the health of the nation if they work together as closely as possible. There is a definite risk of the general practitioners and the hospitals drifting apart, so that any contacts between the two should be fostered. And here is a natural link, between the practitioner and the pathologist; it could only be to the mutual benefit of the two and of the Health Service that this link should be forged and strengthened.

Will the Pathologist be Overwhelmed?

It is common knowledge that the extent to which the pathology service is being used by the general practitioner varies greatly in different parts of the country. In some areas it flourishes, whereas in others it has hardly made a beginning; this has been attributed to the reluctance of the pathologist to encourage the practitioners to use his service for fear of being overwhelmed with a flood of work beyond the resources of his laboratory. Those of us who have had experience of this form of service would agree with Sir Allen Daley (1953) that these fears have usually proved unfounded. In defence of the pathologist who has been hesitant to undertake this work it should, however, be pointed out that when the Health Service was formed, since the practitioner work was probably an unknown quantity, the pathologist worked out the establishment of his laboratory on the basis of the hospital work it would have to undertake. He no doubt thought that he could proceed cautiously and increase his staff as the service developed; he was probably not allowed to do otherwise. Now for various reasons, economic as well as the difficulty of getting staff, he could not expand the work of his laboratory very much if he wished, and he is faced with trying to fit a quart measure into a pint pot. So it makes it all the more important for the general practitioners to get in touch with the pathologists in their districts to find out how they are situated and what they can reasonably undertake. When this service is brought to maturity not only will it lighten the load on the hospitals by making it possible to treat more ill people in their homes, but it will bring an added interest to the work of the pathologist and make general practice an even more worth-while career.

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Next article on Clinical Pathology—"The Public Health Laboratory Service," by Dr. M. T. Parker.

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CAPITAL PUNISHMENT FOR MURDER

THE ROYAL COMMISSION'S REPORT

"... to consider and report whether liability under the criminal law in Great Britain to suffer capital punishment for murder should be limited or modified."

Such was the Royal Warrant for the Commission which has been sitting under the chairmanship of Sir Ernest Gowers for more than four years and has now issued its report.[1] Evidence was taken from 117 witnesses in Great Britain—and many more in other countries—from the Archbishop of Canterbury to the Chief Executioner. In its 500 pages the report discusses proposed amendments to the law, the exercise of the royal prerogative, and alternatives to capital punishment. The sections which will be of chief interest to medical readers are those concerning the M'Naghten Rules and concerning methods of execution. This latter subject was added to the terms of reference at the request of the then Prime Minister (Mr. Attlee).

Murder is, in peacetime, the only offence for which the sentence of death is imposed, and the only offence for which the court has no discretion to alter the sentence. The crime may be human and understandable or brutal and callous to an unbelievable degree; it may have been committed in a fit of passion or as the result of premeditation; motives may range from cupidity or lust to pity or despair, but there remains the one penalty.

Categories of Murder

During the last 50 years, in England and Wales, 1,210 persons have been convicted of murder and sentenced to death. Recommendations to mercy were made in 468 cases and reprieves were granted in 555. Murder in this country is slowly declining. The number of murders known to the police has almost consistently fallen since 1900. The years of highest incidence in England and Wales were 1903 (5.14 per million of population) and 1945 (5.11); the incidence was highest also in Scotland in the last year of the second world war. A rising figure since 1941 is for murders in connexion with sexual assault.

The Commission discusses certain categories of murder. It makes no recommendation with regard to infanticide. It is not considered right to provide by law that a mother who kills her child should in no circumstances be adjudged guilty

[1] Royal Commission on Capital Punishment, 1949–53. Report. Cmd. 8932. London: H.M. Stationery Office. 12s. 6d. net.

of murder. Nor does it advise that in suicide pacts the cases which merit sympathy should be taken out of the category of murder; it is a matter for the Home Secretary to consider advising the exercise of the royal prerogative. The same is true of "mercy killings." The plea that women should be exempted is not accepted; it is based on emotion rather than on logic. By a narrow majority the Commission recommends that the statutory age limit below which a person may not be sentenced to death should be raised from 18 to 21.

The M'Naghten Rules

Out of 3,130 persons committed for trial at assizes on the charge of murder during the present century, 1,275 were certified as insane before trial or insane on arraignment, or were found "guilty but insane," and 48 were certified insane on a medical inquiry held after the trial.

The test of responsibility which a jury must apply was laid down in the replies of the judges to the questions of the House of Lords in the M'Naghten case (1843). The M'Naghten Rules have been closely followed by judges where evidence of insanity was disputed, but have been more freely interpreted or even disregarded where insanity was accepted by the prison medical officer and not disputed by the prosecution. Nevertheless, rare cases arise in which the effect of applying the rules is that sentence of death has to be pronounced on a person whom it would be clearly wrong to regard as responsible.

Among the witnesses heard by the Commission the principal exponent of the inadequacy of the N'Naghten Rules was the British Medical Association,[2] which recommended the adoption of a formula for their enlargement, and this was supported by other witnesses, notably by Lord Justice Denning. In the Commission's view the test of criminal responsibility contained in the rules cannot be defended in the light of modern medical knowledge, and it adopts a British Medical Association formula, but expressed rather more shortly as follows:

> "The jury must be satisfied that, at the time of committing the act, the accused as a result of disease of the mind (or mental deficiency) (*a*) did not know the nature and quality of the act or (*b*) did not know that it was wrong or (*c*) was incapable of preventing himself from committing it."

The Commission holds that it would be better to amend the rules in this way than to leave them as they are, but (with three dissentients) that it would be preferable to abrogate the rules altogether and leave the jury to determine whether at the time of the act the accused was suffering from disease of the mind or mental deficiency to such a degree that he ought not to be held responsible.

Medical Inquiries

Another recommendation is that, following more or less the Scottish practice, every person in England and Wales awaiting trial on a charge of murder should be specially examined by two doctors, of whom one at least should be a psychiatrist of standing, not a member of the prison medical service. The prosecution at present relies on the prison medical officer. The Commission does not recommend the appointment of medical witnesses by the courts instead of by the prosecution or defence; such a procedure would have many repercussions beyond murder trials.

The Commission is of opinion that there will continue to be cases where the accused is insane, though the issue was not raised at the trial either by the defence or by the judge, and therefore that the statutory machinery for medical inquiry after conviction should be retained. It is pointed out that these inquiries are not the same as trial by jury: the jury would consider the state of mind of the accused at the time of the offence, but the medical inquiry is directed primarily to his state of mind at the time of examination.

[2] Witnesses on behalf of the British Medical Association were Mr. Neville Faulkes, the late Dr. R. G. Gordon, Dr. T. Rowland Hill, and Dr. E. B. Strauss.

Methods of Execution

In the western world there are four main methods of execution in addition to hanging: electrocution (in 23 States of the U.S.A.); the guillotine (in France and Belgium); lethal gas (in 8 States of the U.S.A.); and shooting (in almost every country for those sentenced to death for offences against the military code). It is curious that hanging, which was originally adopted because it was so degrading, exhibiting the criminal in the most ignominious and abject of postures, and so thought to have a strong deterrent value, should now be defended on the score of being uniquely humane. Prison chaplains say that hanging is to be preferred "to, say, a shot from the hypodermic. . . . If a man is to die let him walk to his death cleanly." Mr. Pierrepoint, the executioner, told the Commission that in his long experience he had known only one instance of struggle. It is easier for a man to show courage and composure in his last moments if the final act required of him is a positive one, such as walking, than if it is a passive one, like awaiting the prick of a needle.

The time elapsing between the entrance of the executioner into the condemned cell and the fall of the lever is normally between 9 and 12 seconds, provided the cell adjoins the execution chamber, as it usually does. In a series of 58 executions at Wandsworth and Pentonville the cause of death was shown to be fracture dislocation of the cervical vertebrae with laceration or crushing of the cord. Such dislocation causes immediate unconsciousness, though the heart may continue to beat for 20 minutes.

Lethal Gas-chamber and Injection Methods

Accounts are given of the procedure of electrocution and of the lethal gas-chamber. With electrocution the interval between leaving the condemned cell and death is two to four minutes. In the gas chamber the prisoner is apparently unconscious within four seconds of entry; certainly unconscious within five, and respiration and heartbeat have stopped within six. The Commission is in no doubt that in respect of the time taken over preliminaries hanging is superior to either of the other methods.

The Commission was impressed by the opinion of the British Medical Association that if an alternative to hanging had to be found (though it did not advocate any change) gassing by carbon monoxide would be best. There are certain objections to this, chiefly on the ground that the prisoner would not become unconscious for at least one minute after the first inhalation. Lethal injection from a hypodermic syringe is an alternative which suggests itself on the ground of humanity, certainty, and decency, though, apparently, it is not adopted in any country. The drug, probably a barbiturate, would be injected into a vein; in about 20 or 30 seconds it would reach the brain, and the prisoner would become unconscious and die a minute or two later. Expert witnesses, however, questioned the practicability of it. It is impossible to give intravenous injection to a person with certain physical abnormalities, and it is never easy to give it except with the co-operation of the subject. It also demands professional skill, and, says the British Medical Association, "no medical practitioner should be asked to take part in bringing about the death of a convicted murderer." The Commission says:

> "We of course respect the attitude of the British Medical Association, but we think they may have magnified its probable consequences. A later medical witness thought the profession would treat the question as one of individual conscience, and not all doctors would feel debarred from giving instruction for such a purpose. Moreover, it is not only within the profession that the necessary skill is to be found."

The difficulty of getting executioners, if it were the only obstacle, would not prove insuperable. The Commission recommends that the question of lethal injection as a substitute for hanging be examined periodically, especially in the light of the progress made in the science of anaesthetics.

The report contains a vast amount of information about the law of murder in many countries, a historical survey of the M'Naghten Rules, and summaries of notable cases.

SCIENTIFIC FILM CONGRESS IN LONDON

[By a Special Correspondent]

The cinematograph film as a source of amusement has for many years been one of the most popular forms of entertainment, but there is still some doubt as to the exact position it will ultimately take as a means of scientific education. Experiments have been made in many countries to advance technique, and the International Scientific Film Association has done excellent work in collating and co-ordinating the results from all over the world. The seventh International Congress, which was organized for the International Association by the Scientific Film Association of Great Britain, was held in London from September 18 to 27 under the presidency of Mr. John Maddison, and was attended by representatives or observers from 40 countries. At the same time the Royal Photographic Society's International Conference was being held and was attended by many of those interested in scientific films. Sir Arthur Elton, President of the British Scientific Film Association, played an important part in the organization of the Congress.

There was a daily continuous showing of scientific films in several different places, and on two evenings there was a gala performance at the National Film Theatre at which representative films from many countries were shown, and very remarkable some of them were. We recall with particular interest one which showed the life history of the locust, how plagues of locusts arise, and how they can be controlled; and another beautiful film which showed the flight of birds in migration. Official notice of the Congress was shown by a formal reception of the delegates by Lord Woolton at Lancaster House, and by short addresses given at the gala performances by Sir Walter Monckton and Sir Stephen Tallents.

Medical Section

There was a special medical section, of which the chairman was Professor H. M. Dekking (Holland) and the vice-chairman Dr. Ronald MacKeith (London). This section held several meetings to discuss technical points, to consider how the moving film might be applied to endoscopy, to examine its application to biology and the problems of forensic medicine, and to determine its value in medical diagnosis. The last-mentioned was perhaps of most use to the medical members. Dr. MacKeith opened the discussion by a general account of the uses of films in medicine, and he was followed by Professor Dekking, who emphasized the limitations of the film in diagnosis. Then came Mr. Denis Browne (London), who gave examples of the proper use of the film in surgical diagnosis but pointed out that films were only of use as a means of investigation leading up to the final mental process of diagnosis. Dr. P. N. Cardew (London) then stressed the importance of a knowledge of the technique of film-production if the best results in teaching were to be obtained, and finally Dr. P. J. Collard (London) gave evidence of the actual value of films in teaching. The general opinion emerged that films can be used with great advantage in teaching medicine and surgery, but they must be regarded only as animated illustrations and reminders; they can never be a substitute for the routine and time-honoured methods of medical education.

The first session of the World Health Organization's newly appointed committee on rheumatism was held in Geneva last month under the chairmanship of Dr. W. S. C. Copeman. The committee deprecated the indiscriminate use of the new hormone remedies and advised that they should be reserved for use by specialists attached to hospital departments and clinics. They recommended that practitioners should be instructed in modern methods of early diagnosis and treatment of rheumatic diseases, and that in under-developed countries young doctors be encouraged to specialize in them.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Christmas Gifts Fund Appeal

Sir,—I shall be most grateful if you will spare space in your columns for me to appeal for donations to the Royal Medical Benevolent Fund to enable us to distribute Christmas gifts to beneficiaries of the fund.

I hope that all members of the profession will contribute towards this extra help at Christmas time, for it is enormously appreciated by doctors and their dependants who have fallen on hard times. The fact that they are remembered by their more fortunate colleagues gives the recipients of gifts even greater pleasure than the gifts themselves, which, however, provide extra comforts or small luxuries for which they have been longing.

I ask subscribers to the fund to spare a little more for this special purpose, and I beg others to become subscribers at the same time as they respond to my present appeal.

Donations and subscriptions should be sent to the secretary of the Royal Medical Benevolent Fund, 1, Balliol House, Manor Fields, Putney, London, S.W.15, and marked "Christmas Gifts."—I am, etc.,

Webb-Johnson,
President,
Royal Medical Benevolent Fund.

Danger of Penicillin Injection

Sir,—At the suggestion of the manufacturers I am reporting a case of severe anaphylaxis to crystalline penicillin.

The day following my reading in the *Journal* about a case of fatal anaphylaxis to penicillin (September 12, p. 605), I had occasion to give 500,000 units crystalline sodium penicillin to a patient with a large boil on the nose. After about five minutes she was walking home and felt ill. The first symptom was swelling of the tongue and gums followed by intolerable itching of the skin in all areas. She managed to reach home, where she collapsed and became unconscious. I was called after about 15 minutes. She was still unconscious but scratching her skin persistently. Her face was swollen almost beyond recognition, and her skin showed a generalized "flare" response. She was cold, clammy, and almost pulseless. Her airway was not obstructed, however, and there was no cyanosis. She gradually regained consciousness after 1 ml. adrenaline hypodermically, but did not fully recover for another 24 hours.

This same lady, some months ago, had 300,000 units procaine penicillin, and afterwards complained of slight facial swelling and faintness. She said on questioning that she usually swelled unduly after cocaine at the dentist. I therefore assumed that she was sensitive to the procaine, and this was supported by the fact that she had three injections afterwards without any reaction at all. This last injection which was followed by such alarming results was the first for some months, though in the past two years she has had three courses of the drug.

I am happy to say that the bacteria responsible for the boil were equally sensitive to the penicillin, and the lesion had completely subsided by the next day.—I am, etc.,

Anglesey. Kathleen Morgan.

Sir,—I have read with interest the paper by Drs. Frank J. Pick and James F. Patterson (*Journal*, September 12, p. 605) and the letter from Dr. E. J. Masters (p. 629), both of which draw attention to the dangers of penicillin injection. I have personally observed two alarming reactions to injected penicillin in my own small practice.

The first was in a woman aged 30, to whom I had given 500,000 units of pure crystalline penicillin G by intramuscular injection. A few minutes afterwards her face became red and visibly swollen and there was severe difficulty in breathing. She was acutely agitated, but gave no indication of a sense of impending death such as occurred in the cases reported by Batchelor *et al.*[1] Fortunately, intravenous diphenhydramine hydrochloride ("benadryl") was immediately available, and 1 ml. was injected into an arm vein without difficulty. Recovery was rapid and was more or less complete in about 10 minutes.

The second case, also in a woman, occurred after intramuscular injection of 600,000 units of a suspension of procaine penicillin. Within one minute she became acutely ill and on the verge of collapse, but did not lose consciousness. She remained calm mentally, but repeated on several occasions that she was about to die, even going so far as to tell me where her next-of-kin could be reached. Neither intravenous diphenhydramine hydrochloride nor adrenaline was immediately available, and she was placed on a couch until she felt able to go home—a matter of about one hour later. In neither of the above cases could a history of previous asthma be obtained.

It would appear that an increasing percentage of the population is becoming hypersensitive to penicillin, and it may be that the number of near-disasters is greater than is commonly supposed. I would therefore suggest with all earnestness that the time is now ripe for urging the powers that be to agree to the release of aureomycin for general use by doctors.—I am, etc.,

Belfast. H. J. Cronhelm.

Reference

[1] *Lancet*, 1951, 2, 195.

Sir,—The great variation in form from case to case in the published reports of severe anaphylactic reactions to penicillin prompts me to report the following case which presented rather bizarre symptoms.

A woman, aged 34, had a course of penicillin injections for puerperal pyrexia 3½ years ago, and a further course one year ago for a carbuncle on the face, without incident. There is no personal or family history of allergy. She was seen late on September 2, 1953, with acute otitis media, and was given an intramuscular injection of 1 mega unit crystalline penicillin with the usual precautions against injection into a vein. One minute later she suddenly collapsed. She remained unconscious for half a minute, then gradually came round, repeatedly expressing her conviction that she was dying. Her pulse, which was almost impalpable during the phase of unconsciousness, became stronger, rate 100/min. with multiple dropped beats. She continued to feel very ill and weak, and after 15 minutes in this state she suddenly developed a very severe low abdominal colic, exacerbations and remissions each occupying about 10 seconds, and each spasm causing her to writhe. It was "like labour pains, not a bellyache." Pulse still 100/min. with multiple dropped beats. This colic continued for half an hour, then ceased suddenly. A few minutes later she seemed normal, with pulse 80/min. and regular. At no time was there any respiratory embarrassment or cyanosis. A syringe containing 1 in 1,000 adrenaline was held in readiness, but was not used.

Twenty-four hours later she commenced to menstruate, ten days before she was due. She has never before had any menstrual irregularity and has never had dysmenorrhoea. Fifteen days later an intracutaneous injection of 4,000 units crystalline penicillin in 0.2 ml. produced no reaction.

I have used penicillin on a considerable scale in doses of this order for five years, often in allergic individuals and several times in acute attacks of asthma precipitated by respiratory infection, without previously encountering a severe reaction.—I am, etc.,

Leeds, 7. G. W. Lewis.

The Diploma in Public Health

Sir,—The course for the D.P.H. is at present under examination by the Society of Medical Officers of Health. Having recently taken the course and engaged in public health work, I was struck by how little the D.P.H. training assisted me in my duties, particularly as so much weight was given to this diploma in advertisements for assistant medical officers of health. I hope that this letter will give rise to helpful, constructive discussion.

A considerable number of meetings were devoted to clinical instruction in infectious fevers. At present, senior medical officers of health are still in many cases in charge of fever hospitals, but it seems likely that as they retire these hospitals will come under the control of consultants appointed by the regional boards, although apparently the Ministry of Health is not yet committed on this subject. Clinical instruction in fevers would appear to be unnecessary if this assumption is correct, since epidemiology is otherwise dealt with.

A major criticism is that the teachers seemed to overlook that we were all graduates, and a great deal of time was spent in studying matter that had been already learned in our undergraduate days. A whole term was given over to visits with sanitary inspectors and health visitors, and to various departments of local authority work, but many of these had already been done in my youth, and a good many others, such as water-works, were not worth a visit. Six visits were made to a venereal disease clinic and only two to a child welfare clinic. One had the impression that much of the work had been inserted to fill out the course to a year, and indeed one of the lecturers was of opinion that the work could be done in one term. Parasitology was covered in four lectures. One of these described the life of the fly in detail, and was completely useless, since all that can be said about the fly in relation to public health can be said in a few words. Other lectures dealt with amoebic dysentery and tapeworms and were identical in content with undergraduate lectures and valueless. These lectures are a relic of past methods of instruction and their retention is unwarranted and probably due to inertia.

A committee has been appointed by the General Medical Council to examine the C.P.H. diploma, which is a necessary preliminary to the D.P.H. This involves the attendance of external examiners, as well as the payment of an examination fee, after only one term's work, and it appears that only in Bristol University do any candidates fail to proceed to the D.P.H.

The average assistant medical officer of health spends most of his time in antenatal, child welfare, and school health work, and if the dead wood was cut out of the present course there would be ample time to deal with these. The physiology of the normal child should be included in the curriculum, and extended clinical instruction should be held at child welfare centres and antenatal clinics. In fact, much of the material treated in the D.C.H. should be included. Medical officers must be trained in London before they are qualified to test intelligence quotients under the Act, but there seems no reason why instruction of this kind should not be carried out in any university and included in the course. It must be added that, although regulations are laid down by the General Medical Council as to subjects which should be included, there is some lattitude in the subjects at different universities, and it may be that some of these suggestions are already practised elsewhere. At the university at which I studied there were courses of instruction in economics and insurance theory, and some time was devoted to the problems of rehabilitation, which are all extra subjects and could well give way to more relevant matter.—I am, etc.,

Gateshead. Max Park.

Breast-feeding in Oxford

Sir,—May we comment briefly on a few of the points raised in the correspondence following our article?

Professor R. S. Illingworth (*Journal*, August 22, p. 441) has suggested that the involuntary exclusion from the Oxford Child Health Survey of babies who had been seriously ill

during the first two months of life may have led to our obtaining an unduly favourable impression of the results of bottle-feeding. If there had been in Oxford a large number of babies who, *as a direct consequence of early weaning*, fell ill before the age of 2 months and either died or continued to have manifest signs of their illness after this age, then such a bias could have been introduced. We have, however, no reason to suppose that such a group of babies existed, nor do we agree that even in such a hypothetical case "the entire results would be invalidated."

We fully agree that breast-feeding, while it lasts, is a valuable protection against enteric, and possibly other, bacterial infections. Other things being equal, therefore, the amount of illness experienced during infancy should vary inversely with the duration of breast-feeding. But if it is argued that breast-feeding diminishes the incidence of illness in the post-weaning period, then clearly evidence must be produced which distinguishes between illnesses occurring before weaning and those occurring later. Unfortunately, the figures cited by Dr. Elenora Simpson (*Journal*, September 12, p. 628) fail to make this distinction. In the Oxford Survey it so happened that the babies who had been breast-fed for longest had above-average illness rates in the post-weaning period. We do not accept this finding at its face value, but we remain, for the present, sceptical of any allegedly superior resistance on the part of formerly breast-fed babies. On the other hand, the psychological advantages of breast-feeding mentioned by Dr. Duncan Leys (*Journal*, August 29, p. 508) fall right outside the scope of our observations and we do not presume to question their existence or importance.

We agree with Dr. F. Charlotte Naish (*Journal*, September 19, p. 674) that a morbidity index which takes into account the severity and length of illness provides a more precise measure of ill-health than one which merely counts cases. But we do not think that such an index would invariably result in greater differentiation of bottle- from breast-fed babies. Records of duration are available for about 70% of the illnesses covered by our study. These incomplete records show that, on average, a baby receiving breast milk recovered from an attack of bronchitis in about two-thirds of the time taken by a baby who was entirely bottle-fed. For gastro-enteritis, however, which occurred more than twice as frequently during bottle-feeding as during breast-feeding, the mean difference in duration only amounted to a decimal part of a day.—We are, etc.,

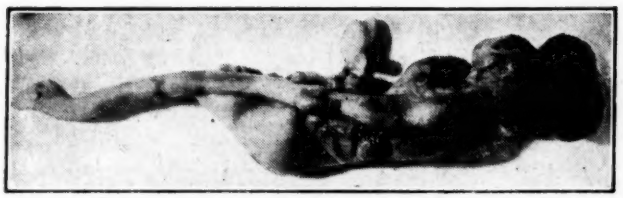
ALICE STEWART.
CELIA WESTROPP.

Oxford.

Inflamed Appendices in Femoral Sacs

SIR,—In view of the letter by Dr. T. E. Winckworth (*Journal*, September 5, p. 567), the following two cases of inflamed appendices in femoral sacs may be of interest.

A housewife, aged 50 years, suddenly noticed a painful lump in the right groin. It appeared to be partly reducible.



It remained tender and of the same size for a week, after which she was admitted to hospital. She was operated on by Mr. G. Myers on November 25, 1948, and a femoral hernia was found, containing a partly strangulated distal half of appendix. The appendix was returned to the abdomen, the sac excised, and the hernia repaired. Laparotomy was performed and a long appendix was removed. It measured 5 in. (13 cm.) in length (see photograph). About its middle was an impression left by the neck of the hernial sac, and below this it was red, oedematous, and inflamed. The patient made a good recovery, but 18 months later a large recurrent hernia appeared and a further repair was performed.

A housewife, aged 57 years, had an attack of abdominal pain and distension associated with a lump in the right groin two weeks before admission. During the next few days the lump became red and painful and then subsided, leaving a firm swelling 2 in. (5 cm.) in diameter and only slightly tender. At operation on November 17, 1952, a femoral hernia was found to be present. It contained pus and the distal half of an acutely inflamed and adherent appendix, the tip of which had perforated. The sac was excised, and appendicectomy performed through the inguinal incision. The hernal orifice was also repaired and the wound closed with drainage. Recovery was good.

Both these cases were seen within a space of four years. The specimens of both cases are now in the hospital museum.—We are, etc.,

T. D. S. HOLLIDAY.
J. R. A. WHITE.

Penzance.

Reciprocity of Qualifications

SIR,—In any future meeting of medical teachers there is one subject which could well be considered which does not seem to have been touched upon during the first World Conference on Medical Education. It is the lack of a uniform system to indicate that a person is fit to practise generally or specially in medicine in any particular country. Unfortunately, different standards are still required in various countries. However, the present multiplicity of recognized qualifications, registrable and otherwise, within countries is confusing and discourages any reciprocity. In the United Kingdom, especially, the innumerable abbreviations affixed to medical practitioners' names appear senseless, particularly to lay and foreign people.

National diplomas or degrees like those recently begun in agriculture and forestry may be the solution, provided county licensure is avoided—otherwise complex conditions similar to those in North America would arise.—I am, etc.,

HAROLD T. DAVENPORT.

Chester.

Cancer and the Public

SIR,—What value can cancer propaganda bring other than that fear which would drive many that have not got it to the doctor? In the recent inquiry by the British Empire Cancer Campaign as to whether doctors considered it a good thing, the majority were against it (see Lord Horder's letter, *Journal*, July 18, p. 148), and it is as well to realize that those against it were not doctors who were likely to "profit" by the opinion; they prefer to be free from the fear-directed patients. One might think from the propaganda enthusiasts that there was a cure for cancer, and that neither general practitioners nor patients had the sense to recognize cancer; that it needed a specialist to do this. Whereas the truth is that we have no cure, and the patient (including the doctor-patient) recognizes its possibility before any specialist can. Unless the patient goes to the doctor and is able to indicate either local signs or symptoms the specialist cannot find it, even in the sick patient, until the patient is nearly or completely dead. This can be illustrated by the histories of patients who when ill consulted the most renowned specialists and submitted themselves to all the latest forms of treatment. Even when the patient goes to the specialist with the earliest recognizable lesion, though localized surgery is then easier, he cannot truthfully say he can cure, as I know full well. And he ought not to add untruth to the anguish of the patient with advanced lesions by chiding the patient that had she come to him earlier he could have cured her, or by writing to the doctor and suggesting that he had neglected the patient by failing to send her before.

I have seen patients who have knowingly had cancer 7–10 years but have failed to consult the doctor because they

feared the fate of relatives and friends who had sought such aid, and, as Shakespeare recognized, "like the owner of some foul disease, to keep it from divulging, let it feed on the pith of life." Find a cure and there will be no need for propaganda. The major manifestations of syphilis have been abolished even though secrecy and not propaganda has dominated treatment. Neither general practitioners nor patients are the fools our propaganda enthusiasts appear to think them. The death rate from cancer is advancing in spite of all the propaganda and the use of every treatment regarded as efficacious. It is just as prevalent in those cities and countries who use these as in the areas which are "spared" these facilities. It seems to me that cellular pathology as applied to cancer has been responsible for much meddlesome interference and little advance in our knowledge. As long as treatment is based on localized lesions, instead of recognizing localized lesions as manifestations of general disease, we shall not advance. Syphilis was not cured by amputation of gummatous organs or limbs. As with any other antisocial affliction, localized shootings or amputations merely drive the growth underground. And what is this propaganda? Since it is implied that general practitioners do not understand it, is it some rare knowledge to be imparted by the most learned? No, the truth is that the truthful element in it is simple common sense which the ordinary school-leaver could readily grasp and the average person already knows, for the propagandists have not spared the public press for many years.

A well-known surgeon was recently quoted in the public press as saying: "I advise the man who smokes heavily, especially if he is over 40, to have a chest *x*-ray every six months—or preferably every three months—so that the physician can find the cancer, if one develops, while surgery can cure it." Apart from the truth that no one has a right to claim a cure, would it not be wise, if it can be proved that smoking is the certain cause, to prohibit smoking? I say this though the radiologist, the physician, and the surgeon with all their army of specialists and technicians would be deprived of work. If it is admitted that smoking can cause cancer once, surely it can cause it again in the same patient if, and it is a big if, surgery could cure the first lesion. John Hunter recognized the truth when he told us: "To amputate is to mutilate a patient you cannot cure." No advance has yet been made on this knowledge.—I am, etc.,

Birmingham. JAMES F. BRAILSFORD.

The Tutorial System

SIR,—We have heard a good deal lately about the increasingly overcrowded medical curriculum, and of the difficulties of deciding what to include and what to omit.

After second M.B., the difficulties, I venture to suggest, do not arise so much from the growing amount of information as from the curious belief that unless much material is packed into courses of compulsory lectures it will not be learned. The maturing student, normally conscientious and ever aware of the forthcoming examinations, is thus placed in the position of an unwilling and irresponsible schoolboy. Getting "signed-up" for such courses is a regular student preoccupation, for, besides being time-consuming, they rob him of chances of attending extra out-patients, visiting the wards, etc.

Rather than attempting to teach increasing amounts in the classroom, the student could be encouraged to learn for himself and, in addition, be given more time in which to do this. Courageous pruning of lecture courses might be coupled with the introduction of the tutorials urged by Sir Lionel Whitby (*Journal*, August 29, p. 451). Most students, I think, would welcome not only this opportunity for discussion but the directives given to their reading by the selection of given topics for these. Lecture courses, on the other hand, would be the more valuable if allotted a supplementary role to ward teaching and private reading, to fill in an ever-broadening and sometimes bewildering theoretical background.—I am, etc.,

Hull. M. K. STRELLING.

Obituary

S. W. JEGER, M.P., M.R.C.S., L.R.C.P.

A Member of Parliament since 1945, Dr. S. W. Jeger died on September 24 at the age of 55.

Santo Wayburn Jeger was born in London on May 20, 1898, and was educated at University College, Cardiff, and at the London and St. Mary's hospitals, qualifying M.R.C.S., L.R.C.P. in 1923. After qualification he settled in general practice in London. Outside his professional work Jeger was keenly interested in politics, and he played an active part in local government. He was elected to the Shoreditch Borough Council in 1925, subsequently becoming chairman of the public health committee, and in 1930 he was elected mayor of the borough. From 1931 to 1946 he was a member of the London County Council and served on its hospitals and public health committees. In 1937 he paid two visits to Spain during the civil war to advise the republicans on medical aid work. During the last war he was medical officer in charge of a mobile ambulance unit and a first-aid post. He was one of the founders of the Socialist Medical Association.

Elliott and Fry, Ltd., London

Jeger was first returned to Parliament at the General Election in 1945, when he was elected Labour Member for St. Pancras South-east, a constituency he had unsuccessfully contested in 1935. At the General Elections in 1950 and 1951 he retained his seat in Parliament as the representative of Holborn and St. Pancras South.

W. LANGMUIR WATT, C.M.G., M.D.

Colonel Langmuir Watt, who was at one time surgeon to the radiotherapy department at Guy's Hospital, died at his home at Victoria, British Columbia, on August 14 at the age of 77.

Walter Langmuir Watt was born at Walkerton, Ontario, on July 12, 1876, and was educated at Manitoba University, where he was a medallist in arts and medicine. After graduating M.D., C.M. in 1898, he continued his medical studies at Dublin, where he obtained the diploma of L.M. at the Rotunda Hospital in 1901, and at Edinburgh, taking the Scottish triple qualification in 1907. For some time before the outbreak of war in 1914 he was in charge of the *x*-ray and electrotherapeutics department of Winnipeg General Hospital, but in August of that year he was mobilized with the Canadian Army Medical Corps, which he first entered in 1902, being commanding officer of the 16th Cavalry field ambulance for many years. Serving throughout the first world war, he attained the rank of colonel, was mentioned in dispatches, and was appointed C.M.G. in 1918.

After the war he settled in practice in London, and in 1925 was appointed assistant surgeon to the actino-

therapy department at Guy's Hospital, where the high-voltage *x*-ray treatment unit for research work, provided at his own expense, demonstrated in a most striking manner its enormous powers for the relief and possible cure of cancer and of serious diseases of the blood. Later the unit was incorporated in the radiotherapy department, to which he became consulting surgeon. He retired from the active staff of the hospital, under the age limit, in 1937, but continued to practise in London until after the end of the second world war, when he returned to Canada. He married Miss Violet Clarke in 1916, and she survives him, together with the son and daughter of the marriage.

Professor Maxime Laignel-Lavastine, the distinguished French psychiatrist and medical historian, died in Paris on September 5. Born at Evreux on September 12, 1875, he received his medical education in Paris, where he qualified in 1903. At the Hôpital Laennec he was chef de clinique médicale from 1904 to 1907, and in 1919 was appointed chef de service. His early interests lay in neurology and psychiatry, and his many publications in this field include *La Méthode Concentrique dans l'Etude des Psychonévroses* (1928), which was translated into English in 1931. He later turned to the study of medical history and was appointed professor of the history of medicine at Paris in 1931. He was co-author of *Les Maladies de l'Esprit et leurs Médecins du XVII au XIX Siècle* (1930), and with Molinery he wrote a short history of French medicine, which in 1934 appeared in translation in the *Clio Medica* series. He edited the superbly produced three-volume *Histoire Générale de la Médecine* (1934–49). Laignel-Lavastine was elected a member of the Académie de Médecine in 1936, and was made an officer of the Legion of Honour in 1939. He was president of the Société Internationale d'Histoire de la Médecine and of the Ligue de Défense de l'Homme contre le Crime. He was on his way from Paris to preside over the Second International Congress of Hippocratic Medicine at Evian when he had a fatal coronary thrombosis.

Medico-Legal

ANAESTHETIST'S RESPONSIBILITY

The administration of a general dental anaesthetic is ruled to be the responsibility of the anaesthetist and not the dentist. The London Executive Council has had before it a case in which a dentist extracted the wrong tooth from a patient who was given a general anaesthetic by an anaesthetist. The dentist, while very much regretting the occurrence, said that in his opinion it was due to the unaccountable nervousness of the anaesthetist. The Dental Services Committee, after hearing the case, expressed its opinion in the following terms:

"There was an unavoidable breach of the Terms of Service in connexion with the administration of the general anaesthetic, and, although the fault lay primarily with the anaesthetist, the responsibility for the treatment of the patient nevertheless rests with the respondent [dental] practitioner."

The executive council communicated this to the Ministry of Health, and the Ministry responded with this contrary opinion:

"The Minister has noted and agrees with the recommendation of the council, except with regard to the findings that there was a breach of the Terms of Service. In this connexion . . . the Minister is advised by his lawyers that under the regulations the dentist is not responsible for the acts and omissions of the anaesthetist and that any person who suffers injury at the hands of the anaesthetist should be left to his civil rights for a remedy."

The Services

Colonel W. R. Ward, T.D., Q.H.S., late R.A.M.C., T.A., has been appointed Honorary Colonel of a T.A. unit in succession to Major-General R. E. Barnsley, C.B., M.C., late R.A.M.C., whose tenure has expired.

A *Supplement* to the *London Gazette* has announced the following awards:

First Clasp to the Territorial Efficiency Decoration.—Colonel W. R. Ward, T.D., late R.A.M.C., Lieutenant-Colonel (Honorary Colonel) E. J. G. Glass, T.D., Lieutenant-Colonel and Brevet Colonel O. G. Prosser, M.C., T.D., Lieutenant-Colonel A. E. K. Price, T.D., Major (Acting Lieutenant-Colonel) R. R. Davies, T.D., Majors J. O. McCarter, F. C. Mayo, T. R. W. Millar, T.D., J. H. Pattyson, T.D., H. R. Shields, B. St. J. Steadman, T.D., and Captain (now Temporary Major, S.S.R.C.) D. R. Hood, R.A.M.C.

Territorial Efficiency Decoration.—Majors (Honorary Lieutenant-Colonels) D. A. Hunt and A. J. Moffett, Majors J. O. McCarter, F. C. Mayo, H. R. Shields, W. J. Street, Captains (Honorary Majors) H. L. Cohen (retired) and W. H. Stephen, Captain (now Temporary Major, S.S.R.C.) D. R. Hood, and Captains H. C. W. Baker and S. S. B. Gilder, R.A.M.C.

Universities and Colleges

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the College held on July 15, with Professor Walter Mercer, President, in the chair, the following were admitted Fellows of the College without examination: Professor Harold Robert Dew, F.R.C.S., F.R.A.C.S., Professor Robert Walmsley, M.D.

At the same meeting the following candidates, having passed the requisite examinations, were admitted Fellows: I. A. Agjee, A. M. Akram, M. A. Uddin, V. Benatar, A. C. Boonzaier, H. D. Bulos, Anne M. Calder, B. M. Chatterjee, S. Chinnatamby, B. H. Colman, D. J. Currie, D. S. Desai, R. B. Duthie, E. C. Eadie, Stella P. Eadie, H. H. Francis, R. Ger, V. N. Larsen, C. W. Law, K. H. Macdonald, J. M. Moore, A. Moselhi, W. J. Oram, J. R. S. Paterson, R. E. Peasegood, J. K. M. Quartey, W. L. Robinson, S. Schwartz, M. Shaffi, S. Sher, K. Y. Shrikhande, H. B. Torrance, H. T. V. Reddi, P. Vulfsons, R. le S. van der Riet.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

The following candidates were duly admitted licentiates in medicine and midwifery on July 3, having passed the final examination in medicine, surgery, and midwifery of the Conjoint Board of Ireland: B. D. Amarasingham, J. J. Biezenski, P. J. Bofin, Eleanor R. Comyn, M. G. Connell, T. A. I. Cunningham, F. T. Daly, R. K. Doyle, H. W. Eldemire, I. J. Fiberesima, P. W. Ford, C. W. Gale, T. U. Glasspole, A. J. Grehan, T. Kirkwood-Hackett, B. P. Harkin, P. J. G. Henry, T. E. C. Jarrett, Zofia Jedliczka, R. Kachan, H. Levison, Barbara Lipowska, D. Lynch, R. B. Macaulay, G. C. Martin, M. J. Murphy, A. Mutchnik, Joan McGill, E. H. Noble, G. A. Obiora, L. O'Brien, C. L. O'Connell, N. O'Connor, T. O'Keeffe, K. N. Oji, K. Ramouthar, D. Stachiewicz, M. O. Thomas, Madeline G. P. Thomson, O. A. Tomlinson, S. W. Wajdenfeld, F. H. Walter.

ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

At the annual meeting of the College held at Hobart in March, with Dr. Alex Murphy, the President, in the chair, the following were elected to the Fellowship: Dr. Ruthven Blackburn, Dr. J. T. Cahill, Dr. M. V. Clarke, Dr. R. G. de Crespigny, Dr. E. B. Durie, Dr. T. H. Steel, Dr. I. M. Wartzki, Dr. S. W. Williams, and Dr. F. Hales Wilson.

The following, having satisfied the Board of Censors in New Zealand, were admitted to the Membership: Dr. K. E. Eyre, Dr. L. G. Hannah, Dr. M. J. Murray, Dr. J. L. Newman, and Dr. G. H. Robertson.

At a meeting of the Council held at Melbourne on May 30, the following, having satisfied the Board of Censors in Australia, were admitted to Membership by the President: Dr. D. E. Anderson, Dr. Peter Bull, Dr. F. Harding Burns, Dr. Eugene G. Galea, Dr. Bryan Gandevia, Dr. R. A. Joske, Dr. J. B. Hickie, Dr. D. A. Hicks, Dr. W. M. Moore, Dr. J. L. Stubbe, Dr. H. P. B. Harvey, Dr. J. D. McDonald, Dr. J. A. W. Kelly, Dr. J. S. Calder, Dr. S. C. Milazzo.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **September 12** (No. 36) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	19	1	5	0		23	4	8	1	1
Dysentery	204	24	126	1	5	132	17	120	4	4
Encephalitis, acute	4	0	0	0		5	1	0	0	1
Enteric fever: Typhoid	6	1	0	0		7	0	0	0	1
Paratyphoid	11	0	1 (B)	0	2 (B)	41	1	1 (B)	1	
Food-poisoning	244	35		0		200	22		1	
Infective enteritis or diarrhoea under 2 years				17	46				20	64
Measles*	603	19	35	18	21	2,937	280	38	31	98
Meningococcal infection	25	0	18	1		28	1	16	0	
Ophthalmia neonatorum	41	3	4	0		55	3	15	0	
Pneumonia†	169	7	145	5		228	11	162	10	
Poliomyelitis, acute: Paralytic	92	4	20	7	9	115	16	22	9	1
Non-paralytic	81	6				73	12			
Puerperal fever§	223	37	15	1		260	36	14	0	
Scarlet fever	505	28	132	24	33	557	44	156	11	28
Tuberculosis: Respiratory			111	28				121	19	
Non-respiratory			20	1				9	6	
Whooping-cough	3,708	280	344	31	30	1,831	132	89	54	116

DEATHS in Great Towns	1953					1952				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0		0	0	0	0		0	1
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0		0		0	0		0	
Infective enteritis or diarrhoea under 2 years	11	0	3	2	2	6	0	2	1	0
Influenza	1	0		0	0	4	0		0	1
Measles				0	0		0		0	0
Meningococcal infection		0					0			
Pneumonia	105	6	19	8	3	116	15		4	3
Poliomyelitis, acute	4	0			0	13	1			0
Scarlet fever		0		0	0		0		0	0
Tuberculosis: Respiratory	78	6	15	4	5	78	9	10	1	8
Non-respiratory		1	2	0	1		1	1	2	1
Whooping-cough	9	1		0	0	1	0		0	0
Deaths 0–1 year	214	23	21	14	15	171	11	20	9	14
Deaths (excluding stillbirths)	4,128	524	519	128	147	3,912	549	512	96	138
LIVE BIRTHS	7,360	1047	787	205	366	7,117	1004	811	212	457
STILLBIRTHS	154	20	21			179	28	20		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Poliomyelitis

Poliomyelitis notifications (uncorrected) in the week ending September 19 (37th week of the year) were as follows: paralytic, 123 (92); non-paralytic, 104 (81); total, 227 (173). This is an increase of 54 compared with the previous week, the figures for which are in parentheses. The increase is largely accounted for by cases in Coventry C.B. and Kettering M.B., in both of which places there has been an abnormally high incidence of the disease. There is little reason to believe that the rise is more than temporary or that the seasonal recession will not be resumed shortly.

Poliomyelitis at Coventry

The incidence of poliomyelitis at Coventry is higher than previously recorded, and the form of the disease is the most severe known there. We are indebted to Dr. T. Morrison Clayton for the following information. In 1950 and 1951 the incidence was rather high in Coventry, with 82 cases in the first year and 98 in the second, of which 21 and 9 cases respectively were paralytic. In 1952 there were 21 cases, 4 of them paralytic. In the present year up to September 26 there have been 152 cases, 91 of them paralytic. There has so far been only one death. The age incidence of the cases notified from June 13 to September 26 is shown in the Table below.

Age	Paralytic	Non-paralytic	Total
0–4	17	19	36
5–9	22	24	46
10–14	8	5	13
15–19	6	3	9
20–29	18	6	24
30+	20	4	24
Total	91	61	152

Industrial Accidents and Diseases

The number of workpeople (other than seamen) in the United Kingdom whose deaths from accidents in the course of their employment were reported in August was 114, compared with 117 in the previous month and 81 in August, 1952. The number of cases of industrial disease reported was 23, including lead poisoning 1, anthrax 3, epithelioma-tous ulceration 11, and chrome ulceration 5. There were no deaths.—*Ministry of Labour Gazette*, September, 1953.

Infectious Diseases

The largest fluctuations in the trends of infectious diseases in England and Wales during the week ending September 12 were decreases in the number of notifications of 350 for whooping-cough, from 4,058 to 3,708, and 199 for measles, from 802 to 603.

The incidence of measles after reaching the highest level ever recorded in the beginning of this year has now declined to the lowest for almost eight years. During the week reviewed the only large variation in the returns of measles was a fall of 83 in the number of notifications in Lancashire, from 187 to 104. The largest falls in the notifications of whooping-cough were 82 in Lancashire, from 337 to 255, 74 in London, from 354 to 280, and 61 in Yorkshire West Riding, from 321 to 260. The number of notifications of scarlet fever were 505, being 22 more than in the preceding week, and no changes of any size were reported in the local trends. 19 cases of diphtheria were notified, 1 fewer than in the preceding week. The chief features of the returns of diphtheria were a rise in Cheshire from 0 to 3 and a fall in Devonshire from 4 to 1.

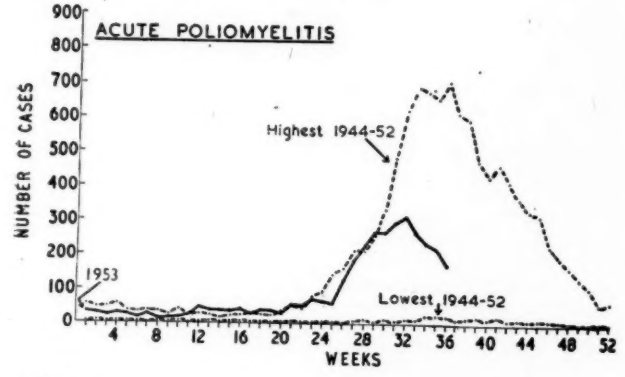
173 cases of acute poliomyelitis were notified during the week. These cases were 31 fewer for paralytic and 20 fewer for non-paralytic cases than in the preceding week. The largest centres of infection were Warwickshire 14 (Coventry

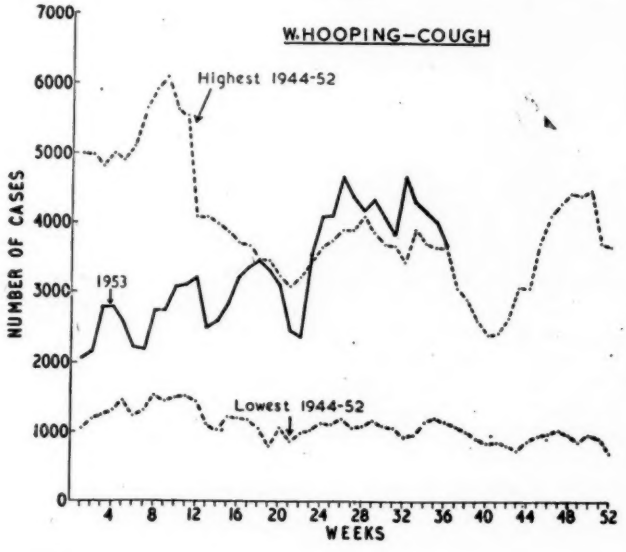
C.B. 6), Dorsetshire 13 (Poole M.B. 4), Yorkshire East Riding 11 (Kingston-upon-Hull C.B. 4, Beverley M.B. 4), London 10 (St. Pancras 6), Southampton County 10 (Bournemouth C.B. 3), Yorkshire West Riding 9 (Leeds C.B. 3), Lancashire 9, and Northamptonshire 9 (Kettering M.B. 8).

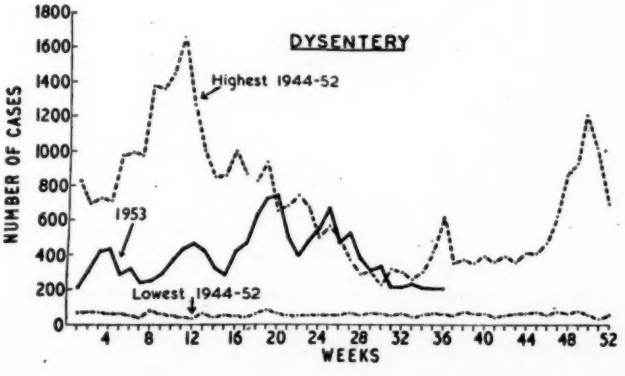
204 cases of dysentery were notified during the week, 1 fewer than in the preceding week. The largest returns were Lancashire 33 (Manchester C.B. 7), Nottinghamshire 30 (Southwell R.D. 26), London 24 (Chelsea 8), Yorkshire West Riding 22 (Bradford C.B. 12), Middlesex 19 (Ealing M.B. 5), and Cheshire 17 (Birkenhead C.B. 17).

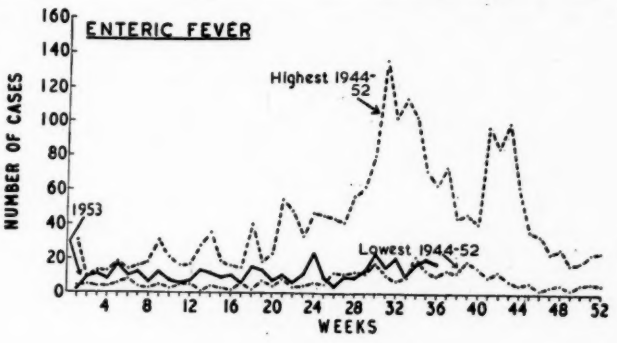
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Quarterly Returns for Scotland

The birth rate during the second quarter of 1953 in Scotland was 18.6 per 1,000, and was 0.8 below the average of the five preceding June quarters. The infant mortality rate was 29 per 1,000 registered live births; this rate was 5 below that for the corresponding quarter of 1952 and 8 below the five years' average, and was the lowest rate ever recorded for any quarter in Scotland. The general death rate was 11.2 per 1,000, being the same as the rate in the preceding June quarter but 0.4 below the five years' average. 278 deaths were ascribed to respiratory and 34 to other forms of tuberculosis, giving rates of 22 and 3 per 100,000 of the population. These rates were respectively 25 and 5 below the average of the five preceding second quarters. 84 deaths were attributed to the principal infectious diseases, being 13 fewer than in the June quarter of 1952. The deaths included in this heading were 50 from influenza, 14 from measles, 13 from whooping-cough, and 7 from meningococcal infections. The death rate from malignant neoplasms was 194 per 100,000, and was 9 above the five years' average.

Week Ending September 19

The notifications of infectious diseases in England and Wales during the week included scarlet fever 633, whooping-cough 3,555, diphtheria 25, measles 608, dysentery 202, paratyphoid fever 8, typhoid fever 6, and food-poisoning 280.

Medical News

Cancer Education.—The Standing Advisory Committee on Cancer and Radiotherapy and the Central Health Services Council have advised the Minister of Health that he should encourage local authorities and voluntary bodies to carry out exploratory schemes of cancer education to enlarge the knowledge of what can be done in this field. Accordingly the Minister of Health has sent a circular (18/53) to local health authorities suggesting that they should consider initiating cancer-education schemes through the medical officer of health, and he draws attention to the model scheme prepared by the Central Council for Health Education. Any authority considering such a scheme must first secure the co-operation of the general-practitioner and hospital services of the area, and the circular states: "Early contact with general practitioners is of particular importance and an invitation should be given to general practitioners to be represented on any committee formed in carrying out work on cancer education." The Minister considers it important that the results of exploratory schemes of cancer education should be carefully and accurately assessed, and the circular enumerates some points on which information would be especially valuable. Regional hospital boards have been asked to assist local authorities with their schemes and to do what they can to achieve the proper registration and follow-up of all cases.

No Change of Name.—At an extraordinary general meeting on September 17 the Society of Medical Officers of Health debated a special resolution to change the name of the society to "The Society of Preventive Medicine."

Dr. Andrew Topping, the retiring president, who was in the chair, said that this question had been before the society for many years, but no satisfactory alternative name had suggested itself until last year, when a joint meeting of the county and county borough groups had declared itself in favour of bringing the phrase "preventive medicine" into the title. To make this change would require a two-thirds majority at an extraordinary general meeting. A postal vote had already been taken, with 937 votes in favour of the change and 160 against it. One reason for the change was the alteration in the composition of the society during the last twenty years. There was not now a preponderance of statutory medical officers of health. After a short discussion, in which Dr. G. W. Fleming (Gosport) urged a combined name, Dr. T. Ruddock-West (Norwich), Dr. Tudor Lewis (Wandsworth), and Professor Leslie Banks (Cambridge) spoke against the change, and Dr. John Yule (Stockport) and Dr. K. Cowan (Chelmsford) supported the change of name, the proposal was defeated by 78 votes to 31. Following the extraordinary general meeting, Dr. C. Metcalfe Brown, medical officer of health for Manchester, was installed as president of the society. He delivered his presidential address on "The National Public Health Service."

W.H.O. European Regional Office.—The Regional Committee for Europe has recommended that the European Regional Office should move to premises in Geneva outside the Palais des Nations, where it has been temporarily housed for the last two years. The World Headquarters of W.H.O. are in the Palais des Nations.

Inquiry into Health Visiting.—The Ministers of Health and Education and the Secretary of State for Scotland have appointed a working party to advise on the proper field of work and the recruitment and training of health visitors in the National Health Service and school health service. The chairman of the working party is Sir Wilson Jameson. The members are Dr. A. Beauchamp, Alderman Mrs. K. Chambers, Miss E. G. Himsworth (nursing supervisor for Midlothian and Peebles), Miss E. Stephenson (chief nursing officer, Newcastle-upon-Tyne), and Dr. J. F. Warin. The inquiry will start this month.

Sir Andrew Davidson, Chief Medical Officer, Department of Health for Scotland, will visit the United States and Canada during November and December. He will be attending various public health conferences, and has accepted invitations to lecture at several American Universities.

COMING EVENTS

College of General Practitioners.—Foundation Membership of the College will close at the first annual general meeting to be held on November 14. Details of this meeting and the annual report will be sent to all members three weeks before the meeting. The following lectures on general practice have been arranged by the College. They will take place at 5.45 p.m. at the Society of Apothecaries, 14, Black Friars Lane, London, E.C.4:

October 8—"Entry into and Setting up in General Practice," by Dr. Geoffrey Barber.
October 13—"The Family Doctor-Patient Relationship," by Dr. George F. Abercrombie.
October 22—"The Present Position and Future of General Practice," by Dr. John H. Hunt.
November 5—"Common Ailments met in General Practice and Seldom Seen in Hospitals," by Dr. Geoffrey Barber.
November 19—"Medical Ethics and the Pitfalls of General Practice," by Dr. Stephen Hadfield.
November 23—"The Running of a Surgery and the Doctor's Round," by Dr. Ian Watson.

Charing Cross Hospital Medical School.—The inaugural address will be delivered by Admiral of the Fleet Sir Philip Vian, G.C.B., K.B.E., D.S.O., at the Royal College of Physicians, Pall Mall East, London, S.W.1, on Friday, October 9, 1953, at 3 p.m. The prizes will be presented by Lady Vian, and Lord Inman will be in the chair.

St. Andrews Medical School, Dundee.—The inaugural postgraduate lecture of the new session will be delivered on October 8 by Sir Russell Brain, P.R.C.P. The title is "Consciousness and Unconsciousness."

The Westminster Medical School.—The inaugural address will be delivered by Lord Radcliffe at Church House, Great Smith Street, London, S.W.1, on October 12 at 3 p.m. Mr. H. M. Clowes will be in the chair.

Princess Tsahai Memorial Hospital Fund.—Mr. Richard St. Barbe Baker will deliver a lecture on behalf of the Fund at the Old Library, B.M.A. House, on October 13 at 3 p.m. Mr. St. Barbe Baker will speak about a recent expedition to the Sahara Desert, and Miss Sylvia Pankhurst will report on the progress of the Princess Tsahai Memorial Hospital. Admission to the lecture will be free, but reserved seats (5s.) may be obtained from the hon. secretary, 3, Charteris Road, Woodford Green, Essex.

1953 Bengué Memorial Award Lecturer.—The Royal Institute of Public Health and Hygiene has appointed General A. M. E. Sicé, M.D., the Bengué Memorial Award Lecturer for 1953. The lecture, entitled "The Evolution of Therapeutics in the Course of the Last Few Years," will be delivered in the Lecture Hall of the Institute, 28, Portland Place, London, W.1, on October 14 at 4 p.m. Admission is free, without ticket.

Course on Allergy.—A course on allergy, comprising theoretical lectures and practical demonstrations, will be held at the Clinique Médicale, Hôpital Broussais, 96, rue Didot, Paris, 14, from October 19 to 29. Applications to attend the course should be sent to the above address; the fee is 5,000 francs for the lectures only, 8,000 francs for the entire course.

Professional Nurses and Midwives Conference.—The 38th annual conference will be held at Seymour Hall, London, W.1, from October 12 to 16, under the presidency of Sir William Gilliatt. Mrs. Iain Macleod will open the conference on the morning of October 12, and the third Blackham Memorial Lecture will be given that day by the Chairman of the Central Midwives Board, Mr. Arnold Walker.

Royal Air Force.—The 23rd annual dinner of the Royal Air Force Medical and Dental Branches will be held at the Hyde Park Hotel, Knightsbridge, London, S.W.1, on Friday, October 23, 1953. All past and present officers who have served in those Branches are eligible to attend. Tickets (27s. 6d. each) may be obtained from Air Ministry (MA3), Awdry House, Kingsway, London, W.C.2.

Manchester Medical Students' Ball.—The Manchester University Medical Students' Representative Council is holding its annual Medical Ball on October 23 in the Whitworth Hall, Manchester University. Application for tickets (price one guinea for a double ticket) should be made to Mr. M. R. Thompson, social secretary of the council, Medical School, The University, Manchester, 13.

The Yorkshire Association of Graduates of Glasgow University will hold its annual dinner on October 23. The guest of honour will be Mr. W. W. Galbraith, P.R.F.P.S. Potential members of the association are asked to communicate with the secretary, Mr. James Wishart, 33, Manor Row, Bradford, 1.

NEW ISSUES

British Journal of Venereal Diseases.—The next issue (Vol. 29, No. 3) will be available in a week's time.

Thorax.—The next issue (Vol. 8, No. 3) will be available in a week's time.

Issued quarterly; annual subscription £2 2s., single copy 12s. 6d.

British Journal of Ophthalmology.—The next issue (Vol. 37, No. 10) will be available in a week's time. Issued monthly; annual subscription £4 4s., single copy 8s. 6d.

These journals are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Applications should be made first to the institution concerned.

Friday, October 2

Whipps Cross Hospital Medical Society.—8.30 p.m., Dr. E. Hinden: Tuberculosis in Childhood.

Monday, October 5

Institute of Psychiatry.—5.30 p.m., Dr. E. Stengel: Lecture demonstration.

London School of Hygiene and Tropical Medicine.—5.15 p.m., Manson Lecture by Sir Rickard Christophers: Malaria in the Field.

● Royal College of Surgeons of England.—5.15 p.m., Mr. Rainsford Mowlem: Role of Surgical Repair in Burns; 6.30 p.m., Mr. Denis Browne: Hirschsprung's Disease.

Tuesday, October 6

Institute of Dermatology.—5.30 p.m., Dr. C. O. Carter: Principles of Genetics.

● Royal College of Surgeons of England.—5.15 p.m., Mr. A. Lawrence Abel: Carcinoma of the Rectum; 6.30 p.m., Major C. K. Anderson: Blood Substitutes.

Wednesday, October 7

Eugenics Society.—At Royal Society, Burlington House, Piccadilly, W., 5.30 p.m., Mr. James Shields: Personality Differences and Neurotic Traits in Normal Twin Schoolchildren.

Institute of Dermatology.—5.30 p.m., Dr. H. Haber: Normal Histology of the Skin.

Institute of Neurology.—5 p.m., Sir Francis Walshe, F.R.S.: Principles of Clinical Neurology.

Institute of Orthopaedics.—8 p.m., clinical-pathological conference.

Manchester Medical Society.—At Medical School, Manchester University, 4.30 p.m. Presidential address by Professor John Morley: A Surgical Retrospect; 8.30 p.m., Reception at Whitworth Art Gallery.

Postgraduate Medical School of London.—2 p.m., Dr. G. H. Algire: Observations on Tissue and Tumour Growth *in vivo*.

● Royal College of Surgeons of England.—5.15 p.m., Mr. V. H. Ellis: Internal Derangement of Joints; 6.30 p.m., Mr. J. M. P. Clark: Some Aspects of Poliomyelitis.

Society of Public Analysts.—At Burlington House, Piccadilly, W., 7 p.m., discussion to be introduced by Dr. G. Roche Lynch: Destruction of Organic Matter.

Yorkshire Society of Anaesthetists.—At Leeds General Infirmary, 8 p.m., Dr. W. D. Wylie: Obstetrical Anaesthesia, with Particular Reference to Cases with Cardiac Disease.

Thursday, October 8

Alfred Adler Medical Society.—At 11, Chandos Street, W., 8 p.m., discussion between psychiatrists and physicians: Psychological Reactions to Physical Disease.

British Postgraduate Medical Federation.—At Beveridge Hall, Senate House, 5.30 p.m., Sir Henry Dale, O.M., F.R.S.: Scientific Method in Medical Research.

● Institute of Child Health and Institute of Neurology.—At National Hospital, Queen Square, W.C., 5.30 p.m., Dr. J. Purdon Martin: Terminology, Diagnosis, Classification, and Physiological Considerations.

London Hospital Medical College.—At Bearsted Theatre, 5 p.m., Schorstein Memorial Lecture by Sir James C. Spence: Varieties of Clinical Experience.

● Royal College of Surgeons of England.—5.15 p.m., Mr. D. J. Robertson: Arterio-venous Fistulae of the Extremities; 6.30 p.m., Mr. Norman C. Tanner: Carcinoma of the Stomach.

St. Andrews University.—At Physiology Department, Dundee, 5 p.m., Sir W. Russell Brain, P.R.C.P.: Consciousness and Unconsciousness.

St. George's Hospital Medical School.—5 p.m., Dr. Denis Williams: Neurology demonstration.

Friday, October 9

Institute of Dermatology.—5.30 p.m., clinical demonstration by Dr. O. L. S. Scott: Developmental Abnormalities.

● Postgraduate Medical School of London.—4 p.m., Sir Neil Hamilton Fairley, F.R.S.: Malaria and its Modern Treatment.

● Royal College of Surgeons of England.—5.15 p.m., Professor Bryan L. McFarland: Reconstructive Surgery of the Hip.

Saturday, October 10

South-East Metropolitan Regional Tuberculosis Society.—At Grove Park Hospital, Marvels Lane, Lee, S.E., 10.30 for 11 a.m., general meeting. "Brains Trust." Speakers, Sir Geoffrey Todd, Dr. James Maxwell, Dr. Thomas C. Wright, and Mr. F. Ronald Edwards.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Collinson.—On September 6, 1953, at Rotherham nursing-home, to Elaine (formerly Micklethwait), wife of John Pexton Collinson, T.D., M.R.C.S., of Burgh-le-Marsh, Lincs, a son—Edward Peter.

Gibson.—On September 7, 1953, to Agnes Macfarlane Stark, M.B., Ch.B., M.R.C.O.G., wife of John Baird Gibson, M.B., Ch.B., D.A., 3, Ewbank Avenue, Newcastle-upon-Tyne—a son.

Rowe.—On August 8, 1953, at Ashleigh Private Hospital, Gosforth, to Sheila (formerly Cowling), wife of Dr. Alan I. Rowe, a son—Simon Inness.

Sloan.—On September 14, 1953, to Mairi, wife of Dr. J. Burnley Sloan, Kelvin Glen, Abbotts Way, Highfield, Southampton, a son—Iain Douglas.

Tighe.—On September 11, 1953, at Birmingham, to Nora (formerly Cregon), wife of John Robert Tighe, M.R.C.S., L.R.C.P., a second daughter—Geraldine Mary.

Vella.—On September 20, 1953, at Cannock, Staffs, to Corinna, wife of Dr. J. M. Vella, a daughter.

DEATHS

Andrews.—On August 22, 1953, at his home, Beechmount, Pittville Circus Road, Cheltenham, Glos, Robin Andrews, M.R.C.S., L.R.C.P., aged 53.

Daman.—On September 3, 1953, in a nursing-home, Lincoln, Thomas Walter Alfred Daman, M.B., C.M.

Hardman.—On September 8, 1953, at Ryde, Isle of Wight, John Leycester Hardman, M.R.C.S., L.R.C.P., late of Nyasaland, aged 31.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Gamma Globulin and Poliomyelitis

Q.—*How does gamma globulin prevent poliomyelitis? Is it a specific effect depending on the donor having developed antibodies to the particular strain of poliomyelitis virus concerned?*

A.—The success of gamma globulin in the prophylaxis or modification of measles is based on the sound assumption that most people have had an attack of measles in childhood, and that the antibodies persist into adult life and are concentrated in the gamma globulin fraction of the plasma proteins. The same assumption has been made in regard to poliomyelitis in the U.S.A., where this infection has been prevalent for the past fifty years, and in fact tests of the gamma globulin prepared from adult donors showed that antibodies to the three main types of poliomyelitis virus were present. It has also been shown that viraemia is a common occurrence in the early stages of poliomyelitis, so that an injection of gamma globulin, containing antibody to the polio virus, at a stage before the virus has become fixed in the nerve cells may be expected—and has proved—to give at least some temporary protection against the infection. In Britain poliomyelitis has occurred in widespread epidemics only since 1947, and it is not yet certain which type or types of the virus are responsible for these recent outbreaks. It would therefore be unwise, and would indeed be impracticable, to use gamma globulin from British donors for the prevention of poliomyelitis in those likely to be exposed to the risk of infection. This matter has been fully discussed in a recent leading article (*Journal*, April 18, p. 874).

Hormones in Cosmetics

Q.—*Various cosmetic preparations, such as "skin foods" and certain hair preparations, are said to contain hormones. Have they any useful therapeutic action, or is their use dangerous?*

A.—Most frequently these cosmetics contain oestrogens in an ointment basis. The inunction of steroid hormones is a recognized therapeutic method of administration, and there is no doubt that the hormone is absorbed into the general circulation. It is possible that the local effect is more concentrated than if given orally or by injection. The effects claimed by the cosmetic sellers, such as "rejuvenation" of skin and abolition of wrinkles, have not been substantiated by any scientific findings. The same is probably true of the scalp hair. This does not mean that oestrogens are not useful under certain recognized conditions—for example, in Simmonds's disease oestrogens are beneficial to scalp hair, restoring its lustre and pigment. In some phases of the climacteric, oestrogens may be indicated.

As to harmful effects, in so far as an oestrogen is a very potent substance even in small doses, and capable of disturbing the rhythm of the menstrual cycle, it is obvious that the use of such preparations may prove harmful quite apart from the controversial question of their potential carcinogenic qualities when administered over long periods. I think it also obvious, from what I have written above, that such preparations should not be used except under the guidance of the patient's physician, who has knowledge of her underlying conditions and of the exact quantities of oestrogen he is prescribing.

There is little doubt that the sale of hormones in shops dealing with cosmetics, and their increasingly widespread

use, is giving rise to considerable anxiety, and that the problem will probably come up for evaluation and guidance under proper auspices. The writer has evidence that disturbing effects are met with, but are usually not reported. He also happened to be a member of a research committee during the war when the question of increasing the milk supply by the administration of oestrogens to cattle was being considered, and the question of the minute amount excreted in the milk was investigated. Contrary to the impression of some clinicians, the very minute amount present in a pint (570 ml.) of milk from an oestrogen-treated cow was sufficient to cause menstrual disturbances in a proportion of a group of female medical students who volunteered to undergo trials for this purpose. The oestrogen for these trials was not administered in milk, but an equivalent amount was given as a tablet.

Repetition of Gold for Rheumatoid Arthritis

Q.—*How often can courses of gold for rheumatoid arthritis be repeated? A patient has had gold (1 g. on each occasion) in 1940, 1949, and 1950 with some benefit. Is a further course indicated?*

A.—Gold is a cumulative drug, but, provided adequate time is allowed for elimination between courses, there is no reason, in the absence of toxic reactions, why courses should not be repeated indefinitely. In the present instance it would seem to be the correct procedure. It is true that in many cases the benefit produced by the initial courses does not seem to be so well reproduced on subsequent occasions. This has led certain workers to advocate the principle of a maintenance dose every few weeks, more or less indefinitely, instead of courses separated by prolonged intervals. One patient who has been satisfactorily maintained in this way for over fifteen years is known to the writer.

Psychological Factors and Myopia

Q.—*Two children, now aged 10 and 11, a brother and sister, have during the last three years suffered from rapid deterioration of their myopia. From the psychological aspect the home environment is highly unsatisfactory. Could this play any part in the deterioration of the children's sight?*

A.—Increase in the amount of myopia during the years of active growth is usual, and there is no known method of preventing such increase. The rate of increase varies among different patients, but tends to be greater in those who display myopia during early childhood. Psychological instability would not be likely to aggravate myopia. Children with more than a dioptre of myopia should wear glasses habitually. Otherwise they miss many beautiful and interesting images during their most impressionable years. Parents should never make depressing remarks about the disadvantage of glasses in the presence of their short-sighted children. Such disadvantages are far outweighed by the handicap of blurred vision, because blurred vision tends to produce clumsiness and lack of confidence.

Pock Marks

Q.—*What can be done to improve the appearance of a patient whose face has been badly disfigured by smallpox?*

A.—The problem of improving the appearance of a face badly disfigured by smallpox or even by acne, which is often just as bad, is a very serious one. The essential difficulty is the pitted surface, and what can be done depends upon the depth and number of the pits. If the pits are single or grouped in such a way that they can be successfully excised, this would be the preferred method; but where they are evenly spread over the face, particularly on the nose, excision is impossible. In such cases, if the scars are not too deep and they do not involve the whole thickness of the skin, considerable improvement can be effected by sandpapering the entire area. This would be equivalent to removing the surface layers of the skin as though a skin graft had been taken from it. For this operation a general anaesthetic is required. When the skin has healed after this somewhat drastic treatment it presents a smoother and more attractive surface. Much the same effect can be produced by performing a face-lifting operation in which the skin is undermined and stretched. These surgical treatments can be applied only occasionally, and it must be regretfully stated that the vast majority of cases of smallpox are not amenable to any form of treatment whatsoever. Cosmetics and various forms of make-up seem to make the condition more apparent.

NOTES AND COMMENTS

Cyclical Buccal Ulceration.—Dr. Katharina Dalton (London, N.22) writes: I note in "Any Questions?" (September 12, p. 634) the history given of cyclical buccal ulceration is typical of the premenstrual syndrome as described by Dr. Raymond Greene and myself in your issue of May 9 (p. 1007). The universally successful treatment of this condition is 50–150 mg. ethisterone daily, or failing this 25 mg. progesterone injections thrice weekly, in the last fortnight of the menstrual cycle. I believe it is the placental production of progesterone during pregnancy that accounts for the almost universal disappearance of this condition during pregnancy.

Our Expert writes: One of the many views about cyclical buccal ulceration is to regard it as a manifestation of the premenstrual or menstrual tension state. It does not, however, respond to treatment as well as do other symptoms of this state, and for this and other reasons the view is not yet widely accepted. On the basis suggested by your correspondent, progesterone, as well as other pregnancy hormones, has been used in treatment for many years, and was advised in the original reply to the question. Ethisterone may be given as a substitute. Dr. Dalton has been fortunate in finding this treatment universally successful, for in the experience of the writer and most other observers it is helpful only in certain cases. Gonadotrophin appears more useful in some cases and oestrogens in others, while many show no beneficial response to any form of sex hormone therapy.

Anaesthesia for E.C.T.—Dr. H. Pullar-Strecker (Isleworth) writes: I do not agree with your expert's opinion ("Any Questions?" August 29, p. 520). It is the preparations that frighten the patient. Having a tooth out with no anaesthetic is all right for other people, but not so good for oneself or one's friends. The same applies for E.C.T.

Correction.—In the article entitled "Blood Transfusion Accidents" (August 15, p. 390) it was stated that the British Red Cross Society has donors on its panels available for giving fresh blood of all groups, at all hours, for planned or emergency work. We have been informed by the British Red Cross Society that these emergency facilities are available only from the Greater London Blood Transfusion Service of the British Red Cross Society.

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